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| | | |
|---|---|---|
| NEWS 1 | | Web Page for STN Seminar Schedule - N. America |
| NEWS 2 | AUG 06 | CAS REGISTRY enhanced with new experimental property tags |
| NEWS 3 | AUG 06 | FSTA enhanced with new thesaurus edition |
| NEWS 4 | AUG 13 | CA/CAplus enhanced with additional kind codes for granted patents |
| NEWS 5 | AUG 20 | CA/CAplus enhanced with CAS indexing in pre-1907 records |
| NEWS 6 | AUG 27 | Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB |
| NEWS 7 | AUG 27 | USPATOLD now available on STN |
| NEWS 8 | AUG 28 | CAS REGISTRY enhanced with additional experimental spectral property data |
| NEWS 9 | SEP 07 | STN AnaVist, Version 2.0, now available with Derwent World Patents Index |
| NEWS 10 | SEP 13 | FORIS renamed to SOFIS |
| NEWS 11 | SEP 13 | INPADOCDB enhanced with monthly SDI frequency |
| NEWS 12 | SEP 17 | CA/CAplus enhanced with printed CA page images from 1967-1998 |
| NEWS 13 | SEP 17 | CAplus coverage extended to include traditional medicine patents |
| NEWS 14 | SEP 24 | EMBASE, EMBAL, and LEMBASE reloaded with enhancements |
| NEWS 15 | OCT 02 | CA/CAplus enhanced with pre-1907 records from Chemisches Zentralblatt |
| NEWS 16 | OCT 19 | BEILSTEIN updated with new compounds |
| NEWS 17 | NOV 15 | Derwent Indian patent publication number format enhanced |
| NEWS 18 | NOV 19 | WPIX enhanced with XML display format |
| NEWS 19 | NOV 30 | ICSD reloaded with enhancements |
| NEWS 20 | DEC 04 | LINPADOCDB now available on STN |
| NEWS 21 | DEC 14 | BEILSTEIN pricing structure to change |
| NEWS 22 | DEC 17 | USPATOLD added to additional database clusters |
| NEWS 23 | DEC 17 | IMSDRUGCONF removed from database clusters and STN |
| NEWS 24 | DEC 17 | DGENE now includes more than 10 million sequences |
| NEWS 25 | DEC 17 | TOXCENTER enhanced with 2008 MeSH vocabulary in MEDLINE segment |
| NEWS 26 | DEC 17 | MEDLINE and LMEDLINE updated with 2008 MeSH vocabulary |
| NEWS 27 | DEC 17 | CA/CAplus enhanced with new custom IPC display formats |
| NEWS 28 | DEC 17 | STN Viewer enhanced with full-text patent content from USPATOLD |
| NEWS 29 | JAN 02 | STN pricing information for 2008 now available |
| NEWS 30 | JAN 16 | CAS patent coverage enhanced to include exemplified prophetic substances |
| NEWS 31 | JAN 28 | USPATFULL, USPAT2, and USPATOLD enhanced with new |

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                  custom IPC display formats
 NEWS 32  JAN 28  MARPAT searching enhanced
 NEWS 33  JAN 28  USGENE now provides USPTO sequence data within 3 days
                  of publication
 NEWS 34  JAN 28  TOXCENTER enhanced with reloaded MEDLINE segment
 NEWS 35  JAN 28  MEDLINE and LMEDLINE reloaded with enhancements
 NEWS 36  FEB 08  STN Express, Version 8.3, now available
 NEWS 37  FEB 20  PCI now available as a replacement to DPCI


 NEWS EXPRESS FEBRUARY 08 CURRENT WINDOWS VERSION IS V8.3,
              AND CURRENT DISCOVER FILE IS DATED 20 FEBRUARY 2008

 NEWS HOURS     STN Operating Hours Plus Help Desk Availability
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 NEWS IPC8      For general information regarding STN implementation of IPC 8

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* * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 20:25:33 ON 22 FEB 2008

=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

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STRUCTURE FILE UPDATES:   21 FEB 2008  HIGHEST RN 1005032-28-9
DICTIONARY FILE UPDATES:  21 FEB 2008  HIGHEST RN 1005032-28-9

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TSCA INFORMATION NOW CURRENT THROUGH January 9, 2008.

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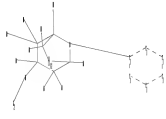
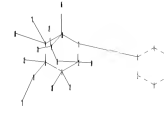
```

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\Stnexp\Queries\10518114allow.str





chain nodes :
13 16 17 18 19 20 21 22 23 24 31
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 14 15
chain bonds :
3-11 7-20 7-21 8-13 8-22 9-17 9-18 10-16 12-19 13-31 14-23 14-24
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 10-14 11-12 12-15
14-15
exact/norm bonds :
1-2 1-6 2-3 3-4 3-11 4-5 5-6 7-8 7-12 7-20 7-21 8-9 8-13 8-22 9-10
9-17 9-18 10-11 10-14 10-16 11-12 12-15 12-19 13-31 14-15 14-23 14-24
isolated ring systems :
containing 1 : 7 :

G1:C,N

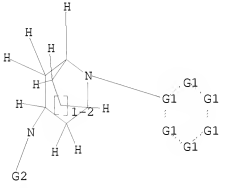
G2:C,H

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:CLASS 14:Atom 15:Atom 16:CLASS 17:CLASS 18:CLASS
19:CLASS 20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 31:CLASS

<12/04/2007> Erich Leese

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR




G1 C,N
G2 C,H

Structure attributes must be viewed using STN Express query preparation.

=> s l1 full
FULL SEARCH INITIATED 20:26:47 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 110328 TO ITERATE

100.0% PROCESSED 110328 ITERATIONS 214 ANSWERS
SEARCH TIME: 00.00.01

L2 214 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 178.82 179.03

FILE 'CAPLUS' ENTERED AT 20:26:52 ON 22 FEB 2008
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FILE COVERS 1907 - 22 Feb 2008 VOL 148 ISS 9
FILE LAST UPDATED: 21 Feb 2008 (20080221/ED)



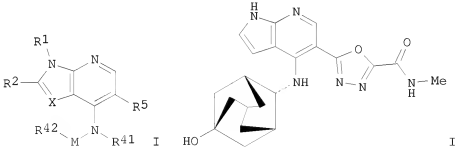
=> s l2 full
L3 19 L2

=> d ibib abs hitstr tot

L3 ANSWER 1 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:757385 CAPLUS
DOCUMENT NUMBER: 147:166304
TITLE: Preparation of heterocyclic compounds as janus kinase 3 inhibitors
INVENTOR(S): Inoue, Takayuki; Tanaka, Akira; Nakai, Kazuo; Sasaki, Hiroshi; Takahashi, Fumie; Shirakami, Shohei; Hatanaka, Keiko; Nakajima, Yutaka; Mukoyoshi, Koichiro; Hamaguchi, Hisao; Kunikawa, Shigeki; Higashi, Yasuyuki
PATENT ASSIGNEE(S): Astellas Pharma Inc., Japan
SOURCE: PCT Int. Appl., 266pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2007077949 | A1 | 20070712 | WO 2006-JP326327 | 20061225 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW | | | | |
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| PRIORITY APPLN. INFO.: | | | JP 2005-378858 | A 20051228 |

OTHER SOURCE(S): MARPAT 147:166304
GI



I II

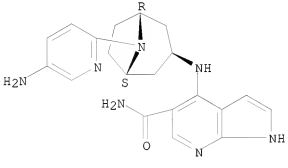
AB The title heterocyclic compds. I [wherein X = N or (un)substituted CH; M = a bond or CH2; R1 and R2 = independently H or (un)substituted alkyl; R41 = H or (un)substituted heteroaryl; R42 = an (un)substituted bridged ring

group; R5 = halo, CN, acyl, etc.; or R41 and R5 form a ring.] or pharmaceutically acceptable salts thereof were prepared as janus kinase 3 (JAK3) inhibitors. For example, II was prepared in a multi-step synthesis. The compds. are useful for treating or preventing various immune diseases, such as rejection during organ/tissue transplantation, autoimmune diseases, multiple sclerosis, rheumatoid arthritis, psoriasis, asthma, etc.

IT 944117-13-9P 944122-15-0P 944122-18-3P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of heterocyclic compds. as JAK3 inhibitors)

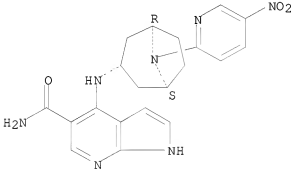
RN 944117-13-9 CAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-(5-amino-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.



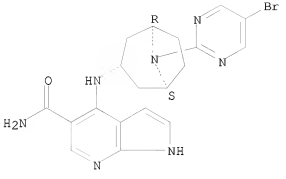
RN 944122-15-0 CAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-(5-nitro-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.



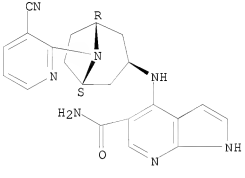
RN 944122-18-3 CAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-(5-bromo-2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.



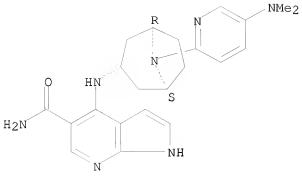
IT 944117-21-9P 944117-22-0P 944117-26-4P
944117-44-6P 944117-52-6P 944118-18-7P
944118-20-1P 944118-46-1P 944121-64-6P
944121-87-3P 944121-88-4P 944121-89-5P
944121-90-8P 944121-91-9P 944121-93-1P
944121-94-2P 944121-98-6P 944122-13-8P
944122-14-9P 944122-16-1P 944122-17-2P
944122-19-4P 944122-21-8P 944122-23-0P
944122-25-2P 944122-26-3P 944122-28-5P
944122-29-6P 944122-31-0P 944122-32-1P
944135-23-3P 944135-24-4P 944135-25-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of heterocyclic compds. as JAK3 inhibitors)
RN 944117-21-9 CAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-(3-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.



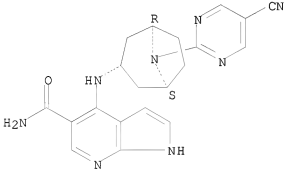
RN 944117-22-0 CAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-[5-(dimethylamino)-2-pyridinyl]-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.



RN 944117-26-4 CAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-(5-cyano-2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.



RN 944117-44-6 CAPLUS
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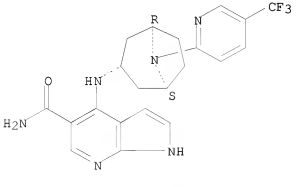
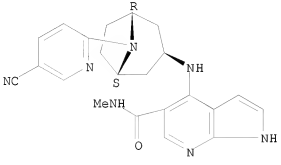
Relative stereochemistry.



RN 944117-52-6 CAPLUS

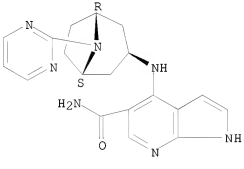
CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]-N-methyl- (CA INDEX NAME)

Relative stereochemistry.



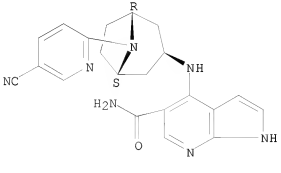

RN 944118-18-7 CAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.




RN 944118-20-1 CAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

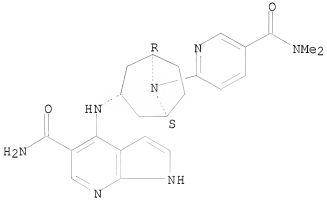
Relative stereochemistry.




RN 944118-46-1 CAPLUS

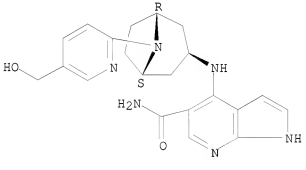
CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-[5-[(dimethylamino)carbonyl]-2-pyridinyl]-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.



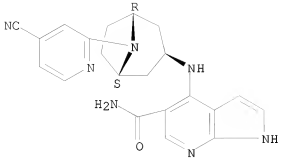
RN 944121-64-6 CAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-[5-(hydroxymethyl)-2-pyridinyl]-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.



RN 944121-87-3 CAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-(4-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.



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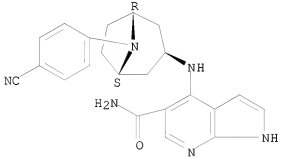
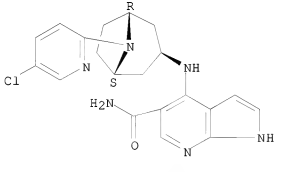
CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-(4-cyanophenyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.



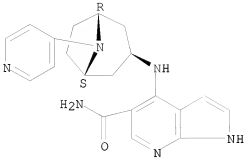
RN 944121-89-5 CAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-(5-chloro-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.



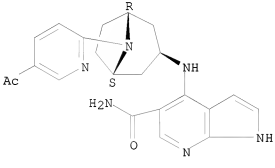
RN 944121-90-8 CAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-(4-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.



RN 944121-91-9 CAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-(5-acetyl-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.

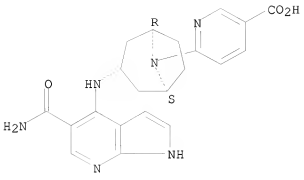


RN 944121-93-1 CAPLUS
CN 3-Pyridinecarboxylic acid, 6-[(3-exo)-3-[[5-(aminocarbonyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]amino]-8-azabicyclo[3.2.1]oct-8-yl]-, 2,2,2-trifluoroacetate (1:3) (CA INDEX NAME)

CM 1

CRN 944121-92-0
CMF C21 H22 N6 O3

Relative stereochemistry.

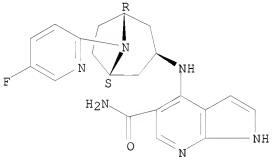


CM 2

CRN 76-05-1
CMF C2 H F3 O2

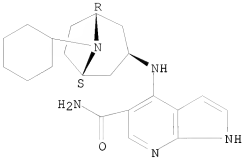
RN 944121-94-2 CAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-(5-fluoro-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.



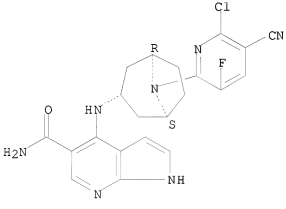
RN 944121-98-6 CAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-cyclohexyl-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.



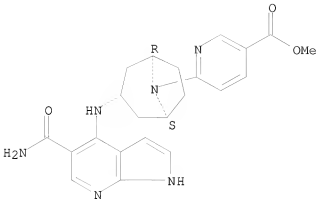
RN 944122-13-8 CAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-(6-chloro-5-cyano-3-fluoro-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.



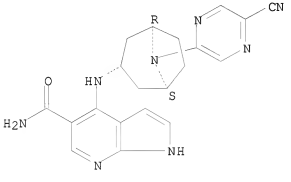
RN 944122-14-9 CAPLUS
CN 3-Pyridinecarboxylic acid, 6-[(3-exo)-3-[[5-(aminocarbonyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]amino]-8-azabicyclo[3.2.1]oct-8-yl]-, methyl ester (CA INDEX NAME)

Relative stereochemistry.



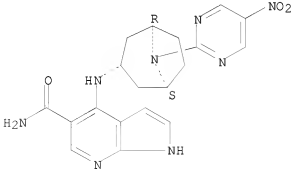
RN 944122-16-1 CAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-(5-cyano-2-pyrazinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.



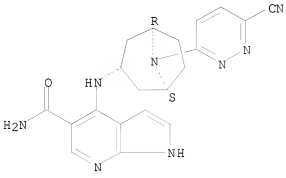
RN 944122-17-2 CAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-(5-nitro-2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.



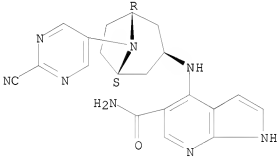
RN 944122-19-4 CAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-(6-cyano-3-pyridazinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.



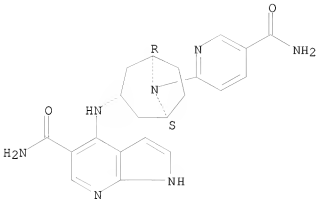
RN 944122-21-8 CAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-(2-cyano-5-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.



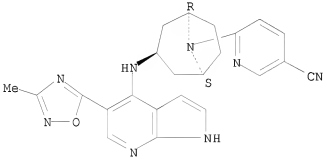
RN 944122-23-0 CAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-[5-(aminocarbonyl)-2-pyridinyl]-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.



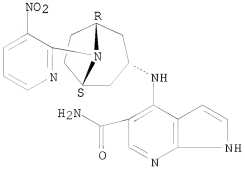
RN 944122-25-2 CAPLUS
CN 3-Pyridinecarbonitrile, 6-[(3-endo)-3-[[5-(3-methyl-1,2,4-oxadiazol-5-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]amino]-8-azabicyclo[3.2.1]oct-8-yl]- (CA INDEX NAME)

Relative stereochemistry.



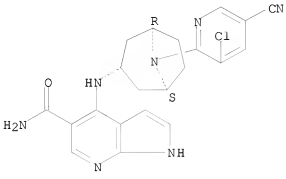
RN 944122-26-3 CAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-endo)-8-(3-nitro-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.



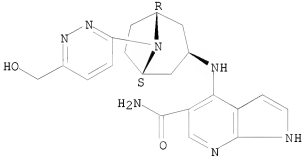
RN 944122-28-5 CAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-(3-chloro-5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.



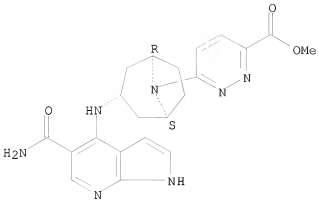
RN 944122-29-6 CAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-[6-(hydroxymethyl)-3-pyridazinyl]-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.



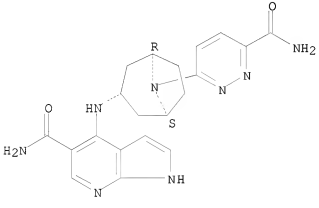
RN 944122-31-0 CAPLUS
CN 3-Pyridazinecarboxylic acid, 6-[(3-exo)-3-[[5-(aminocarbonyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]amino]-8-azabicyclo[3.2.1]oct-8-yl]-, methyl ester (CA INDEX NAME)

Relative stereochemistry.



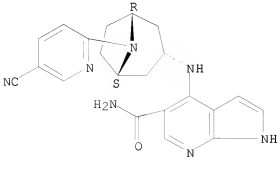
RN 944122-32-1 CAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-[6-(aminocarbonyl)-3-pyridazinyl]-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.



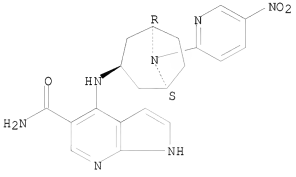
RN 944135-23-3 CAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-endo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.



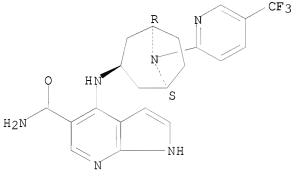
RN 944135-24-4 CAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-endo)-8-(5-nitro-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.



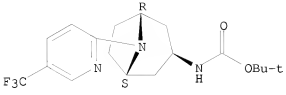
RN 944135-25-5 CAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-endo)-8-[5-(trifluoromethyl)-2-pyridinyl]-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.



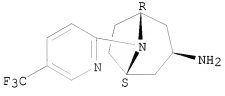
IT 944122-57-0P 944123-89-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of heterocyclic compds. as JAK3 inhibitors)
RN 944122-57-0 CAPLUS
CN Carbamic acid, N-[(3-exo)-8-[5-(trifluoromethyl)-2-pyridinyl]-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (CA INDEX NAME)

Relative stereochemistry.



RN 944123-89-1 CAPLUS
CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-[5-(trifluoromethyl)-2-pyridinyl]-, (3-exo)- (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

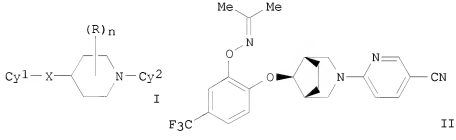
L3 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:409606 CAPLUS
DOCUMENT NUMBER: 146:401834
TITLE: Preparation of azabicyclo[2.2.1]octane derivatives as pesticides
INVENTOR(S): Hamamoto, Isami; Takahashi, Jun; Yano, Makio; Kawaguchi, Masahiro; Hanai, Daisuke; Iwasa, Takao
PATENT ASSIGNEE(S): Nippon Soda Co., Ltd., Japan
SOURCE: PCT Int. Appl., 97pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2007040280 | A1 | 20070412 | WO 2006-JP320126 | 20061006 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

| | | | |
|---|---|---|---|
| PRIORITY APPLN. INFO.: | JP 2005-294126 | A | 20051006 |
| | JP 2005-294127 | A | 20051006 |
| | JP 2005-297803 | A | 20051012 |
| | JP 2005-297804 | A | 20051012 |
| | JP 2006-16877 | A | 20060125 |
| | JP 2006-182314 | A | 20060630 |

OTHER SOURCE(S): MARPAT 146:401834
GI




AB The title compds. I [wherein Cy1 = (un)substituted heterocyclyl; Cy2 = (un)substituted cyclyl, heterocyclyl, etc.; n = 0-9; X = O, S, SO, SO2, or (un)substituted NH; R = OH, halo, (un)substituted NH2, etc.; or two R's

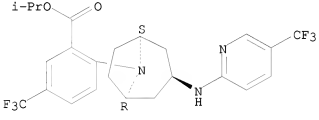
form a ring] are prepared as pest control agents. For example, the compound II was prepared in a multi-step synthesis. Some of compds. I showed excellent pesticidal activities in tests.

IT 933797-20-7P 933797-68-3P 933797-69-4P
933797-70-7P 933797-71-8P
RL: AGR (Agricultural use); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(pesticide; preparation of azabicyclo[2.2.1]octane derivs. as pesticides)

RN 933797-20-7 CAPLUS

CN Benzoic acid, 5-(trifluoromethyl)-2-[(3-endo)-3-[[5-(trifluoromethyl)-2-pyridinyl]amino]-8-azabicyclo[3.2.1]oct-8-yl]-, 1-methylethyl ester (CA INDEX NAME)

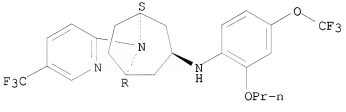
Relative stereochemistry.




RN 933797-68-3 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, N-[2-propoxy-4-(trifluoromethoxy)phenyl]-8-[5-(trifluoromethyl)-2-pyridinyl]-, (3-endo)- (CA INDEX NAME)

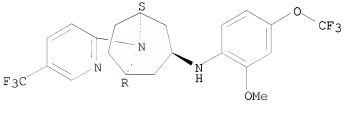
Relative stereochemistry.




RN 933797-69-4 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, N-[2-methoxy-4-(trifluoromethoxy)phenyl]-8-[5-(trifluoromethyl)-2-pyridinyl]-, (3-endo)- (CA INDEX NAME)

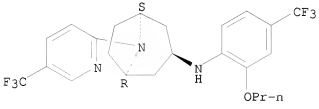
Relative stereochemistry.




RN 933797-70-7 CAPLUS

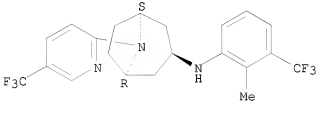
CN 8-Azabicyclo[3.2.1]octan-3-amine, N-[2-propoxy-4-(trifluoromethyl)phenyl]-8-[5-(trifluoromethyl)-2-pyridinyl]-, (3-exo)- (CA INDEX NAME)

Relative stereochemistry.




RN 933797-71-8 CAPLUS
CN 8-Azabicyclo[3.2.1]octan-3-amine, N-[2-methyl-3-(trifluoromethyl)phenyl]-8-[5-(trifluoromethyl)-2-pyridinyl]-, (3-endo)- (CA INDEX NAME)

Relative stereochemistry.




REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

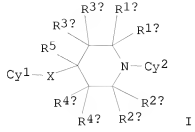
L3 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:405401 CAPLUS
DOCUMENT NUMBER: 146:421857
TITLE: Preparation of bridged cyclic amine compounds as pest control agents
INVENTOR(S): Hamamoto, Isami; Takahashi, Jun; Yano, Makio; Kawaguchi, Masahiro; Hanai, Daisuke; Iwasa, Takao
PATENT ASSIGNEE(S): Nippon Soda Co., Ltd., Japan
SOURCE: PCT Int. Appl., 98pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2007040282 | A1 | 20070412 | WO 2006-JP320133 | 20061006 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

| | | | |
|---|---|---|---|
| PRIORITY APPLN. INFO.: | JP 2005-294126 | A | 20051006 |
| | JP 2005-294127 | A | 20051006 |
| | JP 2005-297803 | A | 20051012 |
| | JP 2005-297804 | A | 20051012 |
| | JP 2006-16877 | A | 20060125 |
| | JP 2006-182314 | A | 20060630 |

OTHER SOURCE(S): MARPAT 146:421857
GI

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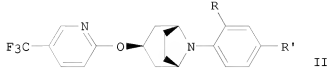



II

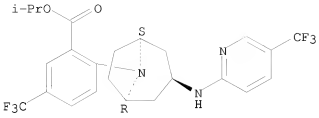
AB Title compds. I [Cy1 = (un)substituted aromatic ring; X = oxygen, sulfur, (un)substituted nitrogen, etc.; R1a and R2a, R1a and R4a, R2a and R3a, or R3a and R4a may combine to form a saturated ring.; R1a-R4a, R1b-R4b and R5 = H, hydroxy, halo, etc.; Cy2 = (un)substituted aromatic ring; when R1a and R2a may combine to form saturated ring and Cy1 is a (un)substituted Ph, Cy2 is a (un)substituted aromatic heterocycle.; when Cy1 is a (un)substituted Ph and Cy2 is a pyridin-2-yl, Cy2 is a pyridin-2-yl substituted with one or more cyano groups.], salts or N-oxides thereof were prepared For example, reaction of tropine with 2-chloro-5-trifluoromethylpyridine followed by treatment with 2,2,2-trichloroethyl chloroformate, reduction using Zn/acetic acid and O-arylation with 2-fluoro-5-trifluoromethylbenzaldehyde afforded compound II [R = CHO; R' = CF3]. Compound II [R = OCH2CH2CH3; R' = CF3] controlled two-spotted spider mite by 100%.

IT 933797-20-7P 933797-68-3P 933797-69-4P
933797-70-7P 933797-71-8P
RL: AGR (Agricultural use); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of bridged cyclic amine compds. as pest control agents)

RN 933797-20-7 CAPLUS

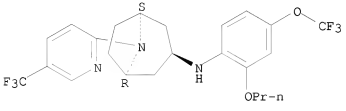
CN Benzoic acid, 5-(trifluoromethyl)-2-[(3-endo)-3-[[5-(trifluoromethyl)-2-pyridinyl]amino]-8-azabicyclo[3.2.1]oct-8-yl]-, 1-methylethyl ester (CA INDEX NAME)

Relative stereochemistry.



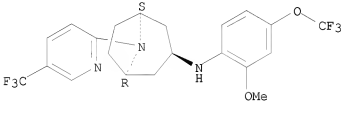
RN 933797-68-3 CAPLUS
CN 8-Azabicyclo[3.2.1]octan-3-amine, N-[2-propoxy-4-(trifluoromethoxy)phenyl]-8-[5-(trifluoromethyl)-2-pyridinyl]-, (3-endo)- (CA INDEX NAME)

Relative stereochemistry.



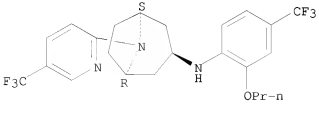
RN 933797-69-4 CAPLUS
CN 8-Azabicyclo[3.2.1]octan-3-amine, N-[2-methoxy-4-(trifluoromethoxy)phenyl]-8-[5-(trifluoromethyl)-2-pyridinyl]-, (3-endo)- (CA INDEX NAME)

Relative stereochemistry.



RN 933797-70-7 CAPLUS
CN 8-Azabicyclo[3.2.1]octan-3-amine, N-[2-propoxy-4-(trifluoromethyl)phenyl]-8-[5-(trifluoromethyl)-2-pyridinyl]-, (3-exo)- (CA INDEX NAME)

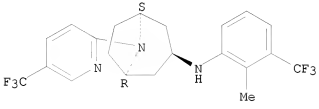
Relative stereochemistry.



RN 933797-71-8 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, N-[2-methyl-3-(trifluoromethyl)phenyl]-8-[5-(trifluoromethyl)-2-pyridinyl]-, (3-endo)- (CA INDEX NAME)

Relative stereochemistry.

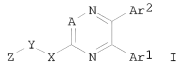



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1124114 CAPLUS
DOCUMENT NUMBER: 145:455030
TITLE: Preparation of substituted heteroaryl CB1 antagonists
INVENTOR(S): Yuan, Jun; Guo, Qin; Zhao, He; Hu, Shaojing; Whitehouse, Darren; Fringle, Wallace; Mao, Jianmin; Maynard, George; Hammer, Jack; Wustrow, David; Li, Hongbin
PATENT ASSIGNEE(S): Neurogen Corporation, USA
SOURCE: PCT Int. Appl., 447pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2006113704 | A2 | 20061026 | WO 2006-US14548 | 20060418 |
| WO 2006113704 | A3 | 20070208 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| CA 2606288 | A1 | 20061026 | CA 2006-2606288 | 20060418 |
| US 2007078135 | A1 | 20070405 | US 2006-406532 | 20060418 |
| EP 1871762 | A2 | 20080102 | EP 2006-750555 | 20060418 |
| R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR | | | | |

PRIORITY APPLN. INFO.: US 2005-672452P P 20050418
WO 2006-US14548 W 20060418
OTHER SOURCE(S): MARPAT 145:455030
GI



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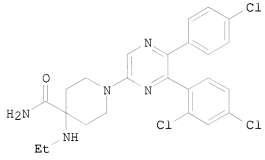


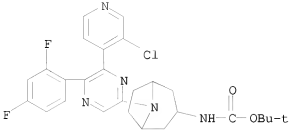
II

AB The title compds. I [A = CR1 or N; Ar1, Ar2 = (un)substituted 5-10 membered carbocycle and heterocycle; X = (un)substituted CH2, O, NH or SOmNH; m = 0-2; Y = (un)substituted alkylene; Z = (un)substituted OH, NH2, SOmNH2, etc.; R1 = H, halo, CN, etc.] which may be used to modulate CB1 activity in vivo or in vitro, and are particularly useful in the treatment of conditions responsive to CB1 modulation in humans, domesticated companion animals and livestock animals, including appetite disorders, obesity and addictive disorders, were prepared E.g., a multi-step synthesis of II, starting from 2,6-dichloropyrazine and 4-(ethylamino)piperidine-4-carboxamide, was given. Exemplified compds. I were tested at CB1 receptor. Thus, II as many other representative compds. I showed IC50 of 2 μM or less. Pharmaceutical compns. and methods for using compds. I to treat disorders responsive to CB1 modulation are provided, as are methods for using such ligands for receptor localization studies and various in vitro assays.

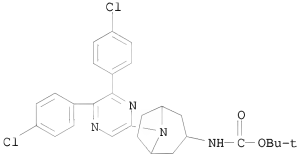
IT 913281-93-3P 913281-94-4P 913281-97-7P
913282-02-7P 913282-12-9P 913282-17-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted heteroaryl compds. useful in treatment of diseases responsive to CB1 activation)

RN 913281-93-3 CAPLUS

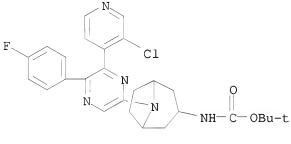
CN Carbamic acid, [8-[6-(3-chloro-4-pyridinyl)-5-(2,4-difluorophenyl)pyrazinyl]-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



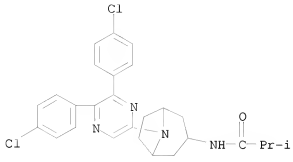
RN 913281-94-4 CAPLUS
CN Carbamic acid, [8-[5,6-bis(4-chlorophenyl)pyrazinyl]-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



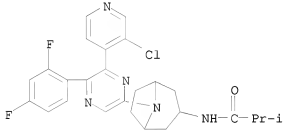
RN 913281-97-7 CAPLUS
CN Carbamic acid, [8-[6-(3-chloro-4-pyridinyl)-5-(4-fluorophenyl)pyrazinyl]-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



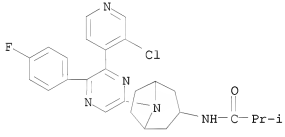
RN 913282-02-7 CAPLUS
CN Propanamide, N-[8-[5,6-bis(4-chlorophenyl)pyrazinyl]-8-azabicyclo[3.2.1]oct-3-yl]-2-methyl- (9CI) (CA INDEX NAME)



RN 913282-12-9 CAPLUS
CN Propanamide, N-[8-[6-(3-chloro-4-pyridinyl)-5-(2,4-difluorophenyl)pyrazinyl]-8-azabicyclo[3.2.1]oct-3-yl]-2-methyl- (9CI) (CA INDEX NAME)



RN 913282-17-4 CAPLUS
CN Propanamide, N-[8-[6-(3-chloro-4-pyridinyl)-5-(4-fluorophenyl)pyrazinyl]-8-azabicyclo[3.2.1]oct-3-yl]-2-methyl- (9CI) (CA INDEX NAME)



L3 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:606621 CAPLUS
DOCUMENT NUMBER: 145:63034
TITLE: Preparation of silicon compounds and their use in medicament
INVENTOR(S): Showell, Graham Andrew; Walsh, Louise Marie; Mandal, Ajay Kumar
PATENT ASSIGNEE(S): Paradigm Therapeutics Ltd., UK
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2006064277 | A1 | 20060622 | WO 2005-GB4905 | 20051216 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| AU 2005315331 | A1 | 20060622 | AU 2005-315331 | 20051216 |
| CA 2590881 | A1 | 20060622 | CA 2005-2590881 | 20051216 |
| EP 1824863 | A1 | 20070829 | EP 2005-820647 | 20051216 |
| R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR | | | | |
| CN 101107259 | A | 20080116 | CN 2005-80043255 | 20051216 |
| IN 2007DN03844 | A | 20070831 | IN 2007-DN3844 | 20070522 |
| KR 2007097468 | A | 20071004 | KR 2007-714460 | 20070625 |

PRIORITY APPLN. INFO.: GB 2004-27722 A 20041217
WO 2005-GB4905 W 20051216
OTHER SOURCE(S): CASREACT 145:63034; MARPAT 145:63034
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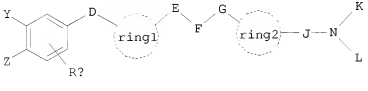


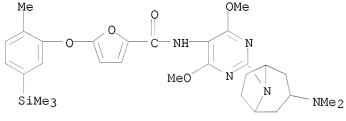

I

AB Preparation of title compds., e.g. I (D = (un)substituted alkylene, O, thionyl, sulfonyl, etc.; E, F, G = same or different (un)substituted alkylene, (un)substituted amino, etc.; J = bond, heterocycloalkyl, etc.; K, L = same or different H, alkyl, cycloalkyl, alkoxy, etc.; Ra, K or L taken together as heterocycloalkyl; Ra = H, halo, alkyl, aryl, hydroxy, alkoxy, etc.; Y, Z = same or different H, halo, alkyl, hydroxy, alkoxy, cyano, organosilyl, etc.; ring1 and ring2 = same or different arylene, heteroarylene optionally substituted with Ra; at least one of Y and Z includes a Si atom), and their use in therapy is described.

IT 891860-56-3P, 5-(2-Methyl-5-(trimethylsilyl)phenoxy)-N-(2-(3-(dimethylamino)-8-azabicyclo[3.2.1]octan-8-yl)-4,6-dimethoxypyrimidin-5-yl)furan-2-carboxamide
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of organosilyl compds. and their use in medicament)

RN 891860-56-3 CAPLUS

CN 2-Furancarboxamide, N-[2-[3-(dimethylamino)-8-azabicyclo[3.2.1]oct-8-yl]-4,6-dimethoxy-5-pyrimidinyl]-5-[2-methyl-5-(trimethylsilyl)phenoxy]- (CA INDEX NAME)



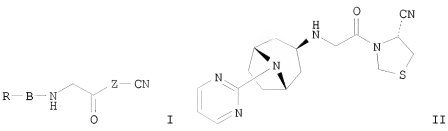

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:1006982 CAPLUS
DOCUMENT NUMBER: 140:59518
TITLE: Preparation of [[(8-azabicyclo[3.2.1]octyl)amino]acetyl]- or [[(9-azabicyclo[3.3.1]nonyl)amino]acetyl]heterocyclic carbonitriles as dipeptidyl-peptidase-IV inhibitors
INVENTOR(S): Aranyi, Peter; Balazs, Laszlo; Bata, Imre; Batori, Sandor; Boronkay, Eva; Kapui, Zoltan; Susan, Edit; Szabo, Tibor; Nagy, Lajos T.; Urban-Szabo, Katalin; Varga, Marton
PATENT ASSIGNEE(S): Sanofi-Synthelabo, Fr.
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003106456 | A2 | 20031224 | WO 2003-HU41 | 20030611 |
| WO 2003106456 | A3 | 20040304 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| HU 2002002001 | A2 | 20050829 | HU 2002-2001 | 20020614 |
| AU 2003244880 | A1 | 20031231 | AU 2003-244880 | 20030611 |
| BR 2003011771 | A | 20050329 | BR 2003-11771 | 20030611 |
| EP 1517907 | A2 | 20050330 | EP 2003-738355 | 20030611 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| CN 1662530 | A | 20050831 | CN 2003-813858 | 20030611 |
| JP 2005532369 | T | 20051027 | JP 2004-513288 | 20030611 |
| NZ 537633 | A | 20060831 | NZ 2003-537633 | 20030611 |
| IN 2004KN01852 | A | 20051230 | IN 2004-KN1852 | 20041206 |
| ZA 2004009907 | A | 20060830 | ZA 2004-9907 | 20041207 |
| KR 756761 | B1 | 20070907 | KR 2004-720277 | 20041213 |
| MX 2004PA12691 | A | 20050815 | MX 2004-PA12691 | 20041214 |
| NO 2005000199 | A | 20050304 | NO 2005-199 | 20050113 |
| US 2005153973 | A1 | 20050714 | US 2005-518114 | 20050321 |

PRIORITY APPLN. INFO.: HU 2002-2001 A 20020614
WO 2003-HU41 W 20030611

OTHER SOURCE(S): MARPAT 140:59518
GI



I II

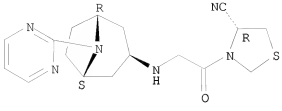
AB Title compds. I [wherein R = (un)substituted N-containing 1- or 2-ring aromatic moieties, p-tolylsulfonyl, R1aCH2, or R1bCO; R1a = H or (un)substituted alkyl, Ph, PhCH2, Ph(CH2)2, PhCH=CH, naphthyl, pyridyl, etc.; R1b = (un)substituted alkyl, Ph, PhCH2, Ph(CH2)2, PhCH=CH, naphthyl, pyridyl, etc.; B = 8-azabicyclo[3.2.1]octyl or 9-azabicyclo[3.3.1]nonyl; Z = thiazolidinediyl, (hydroxy or oxo)pyrrolidinediyl, oxazolidinediyl, or dihydropyrrolidinediyl; and salts, isomers, tautomers, hydrates, or solvates thereof] were prepared as dipeptidyl-peptidase-IV (DPP-IV) inhibitors. These compds. contain tropane building blocks. For example, substitution of tert-Bu 8-benzyl-8-azabicyclo[3.2.1]oct-3-yl-exo-carbamate with 2-chloropyrimidine gave the 8-pyrimidinyl derivative (67%), which was converted to the amine (77%) using TFA. Amidation of (4R)-3-(tert-butoxycarbonyl)thiazolidine-4-carboxylic acid (88%), followed by deprotection (81%), addition of chloroacetyl chloride (75%), and reduction of the amide to the nitrile (43%), gave (4R)-3-(2-chloroacetyl)thiazolidine-4-carbonitrile. Coupling of 8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl-exo-amine with the nitrile using TEA in MeCN afforded II (53%). Compds. of the invention show low IC50 values for DPP-IV enzyme inhibitory activity in comparison with known compds. and are strong, long-acting enzyme inhibitors (no data). Thus, I and their pharmaceutical compns. are useful for the treatment of DPP-IV related diseases.

IT 637018-37-2P 637018-38-3P 637018-39-4P
637018-40-7P 637018-41-8P 637018-42-9P
637018-43-0P 637018-44-1P 637018-45-2P
637018-53-2P 637018-54-3P 637018-55-4P
637018-56-5P 637018-57-6P 637018-58-7P
637018-59-8P 637018-60-1P 637018-74-7P
637018-84-9P 637019-04-6P 637019-05-7P
637330-99-5P 637331-04-5P 637331-18-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of [[(8-azabicyclo[3.2.1]octyl)amino]acetyl]- or [[(9-azabicyclo[3.3.1]nonyl)amino]acetyl]heterocyclic carbonitriles as DPP-IV inhibitors)

RN 637018-37-2 CAPLUS

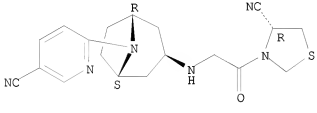
CN 4-Thiazolidinecarbonitrile, 3-[[[(3-exo)-8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 637018-38-3 CAPLUS
CN 4-Thiazolidinecarbonitrile, 3-[[[(3-exo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride, (4R)- (9CI) (CA INDEX NAME)

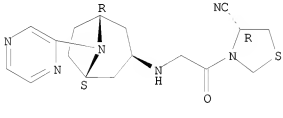
Absolute stereochemistry.



●2 HCl

RN 637018-39-4 CAPLUS
CN 4-Thiazolidinecarbonitrile, 3-[[[(3-exo)-8-pyrazinyl-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride, (4R)- (9CI) (CA INDEX NAME)

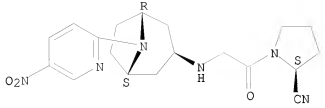
Absolute stereochemistry.



●2 HCl

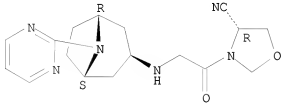
RN 637018-40-7 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(5-nitro-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



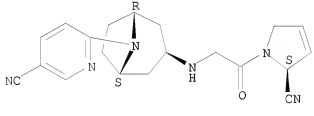
RN 637018-41-8 CAPLUS
CN 4-Oxazolidinecarbonitrile, 3-[[[(3-exo)-8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 637018-42-9 CAPLUS
CN 1H-Pyrrole-2-carbonitrile, 1-[[[(3-exo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-2,5-dihydro-, dihydrochloride, (2S)- (9CI) (CA INDEX NAME)

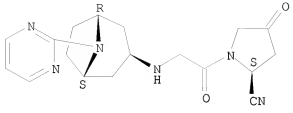
Absolute stereochemistry.



●2 HCl

RN 637018-43-0 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-oxo-1-[[[(3-exo)-8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride, (2S)- (9CI) (CA INDEX NAME)

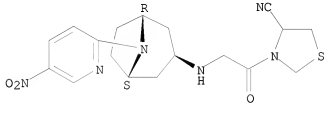
Absolute stereochemistry.



●2 HCl

RN 637018-44-1 CAPLUS
CN 4-Thiazolidinecarbonitrile, 3-[[[(3-exo)-8-(5-nitro-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)

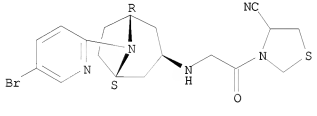
Relative stereochemistry.



●2 HCl

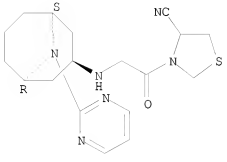
RN 637018-45-2 CAPLUS
CN 4-Thiazolidinecarbonitrile, 3-[[[(3-exo)-8-(5-bromo-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 637018-53-2 CAPLUS
CN 4-Thiazolidinecarbonitrile, 3-[[[(3-endo)-9-(2-pyrimidinyl)-9-azabicyclo[3.3.1]non-3-yl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)

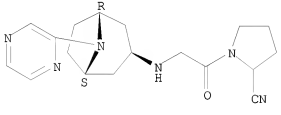
Relative stereochemistry.



●2 HCl

RN 637018-54-3 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-pyrazinyl-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)

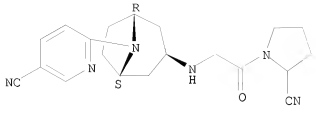
Relative stereochemistry.



●2 HCl

RN 637018-55-4 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)

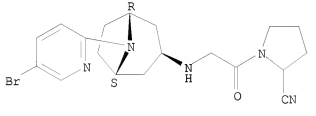
Relative stereochemistry.



●2 HCl

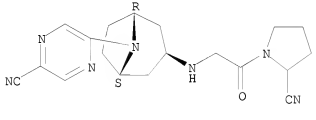
RN 637018-56-5 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(5-bromo-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



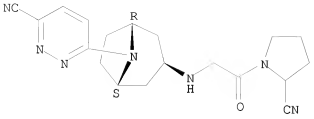
RN 637018-57-6 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(5-cyanopyrazinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



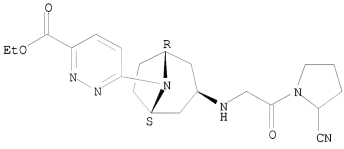
RN 637018-58-7 CAPLUS
CN 3-Pyridazinecarbonitrile, 6-[(3-exo)-3-[[2-(2-cyano-1-pyrrolidinyl)-2-oxoethyl]amino]-8-azabicyclo[3.2.1]oct-8-yl]- (CA INDEX NAME)

Relative stereochemistry.



RN 637018-59-8 CAPLUS
CN 3-Pyridazinecarboxylic acid, 6-[(3-exo)-3-[[2-(2-cyano-1-pyrrolidinyl)-2-oxoethyl]amino]-8-azabicyclo[3.2.1]oct-8-yl]-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

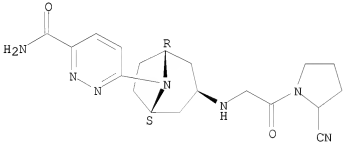
Relative stereochemistry.



● HCl

RN 637018-60-1 CAPLUS
CN 3-Pyridazinecarboxamide, 6-[(3-exo)-3-[[2-(2-cyano-1-pyrrolidinyl)-2-oxoethyl]amino]-8-azabicyclo[3.2.1]oct-8-yl]-, monohydrochloride (9CI) (CA INDEX NAME)

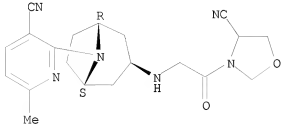
Relative stereochemistry.



● HCl

RN 637018-74-7 CAPLUS
CN 4-Oxazolidinecarbonitrile, 3-[[[(3-exo)-8-(3-cyano-6-methyl-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)

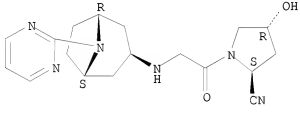
Relative stereochemistry.




●2 HCl

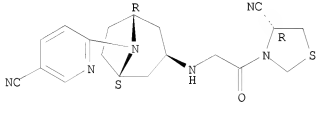
RN 637018-84-9 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-hydroxy-1-[[[(3-exo)-8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, (2S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



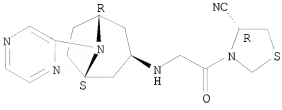

RN 637019-04-6 CAPLUS
CN 4-Thiazolidinecarbonitrile, 3-[[[(3-exo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



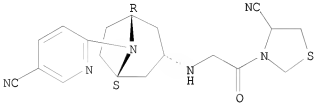

RN 637019-05-7 CAPLUS
CN 4-Thiazolidinecarbonitrile, 3-[[[(3-exo)-8-pyrazinyl-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



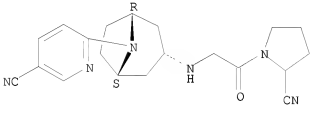
RN 637330-99-5 CAPLUS
CN 4-Thiazolidinecarbonitrile, 3-[[[(3-endo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



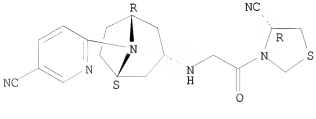
RN 637331-04-5 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-endo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 637331-18-1 CAPLUS
CN 4-Thiazolidinecarbonitrile, 3-[[[(3-endo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, (4R)- (9CI) (CA INDEX NAME)

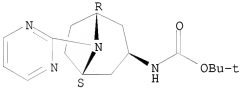
Absolute stereochemistry.



IT 596816-99-8P 596817-00-4P 596817-03-7P
596817-04-8P 596817-10-6P 596817-11-7P
596817-14-0P 596817-15-1P 596817-16-2P
596817-22-0P 596817-37-7P 596817-66-2P
596817-67-3P 596817-70-8P 596817-71-9P
596817-72-0P 596817-78-6P 596817-92-4P
637331-09-0P 637331-13-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of [[(8-azabicyclo[3.2.1]octyl)amino]acetyl]- or [[(9-azabicyclo[3.3.1]nonyl)amino]acetyl]heterocyclic carbonitriles as DPP-IV inhibitors)

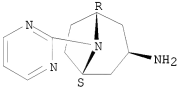
RN 596816-99-8 CAPLUS
CN Carbamic acid, [(3-exo)-8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



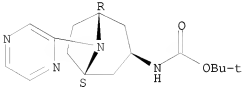

RN 596817-00-4 CAPLUS
CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(2-pyrimidinyl)-, (3-exo)- (CA INDEX NAME)

Relative stereochemistry.



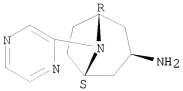

RN 596817-03-7 CAPLUS
CN Carbamic acid, [(3-exo)-8-pyrazinyl-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



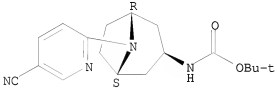

RN 596817-04-8 CAPLUS
CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-pyrazinyl-, (3-exo)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



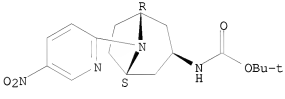
RN 596817-10-6 CAPLUS
CN Carbamic acid, [(3-exo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



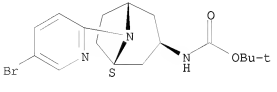
RN 596817-11-7 CAPLUS
CN Carbamic acid, [(3-exo)-8-(5-nitro-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



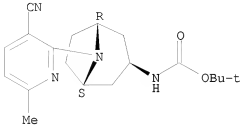
RN 596817-14-0 CAPLUS
CN Carbamic acid, [(3-exo)-8-(5-bromo-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



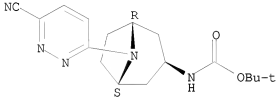
RN 596817-15-1 CAPLUS
CN Carbamic acid, [(3-exo)-8-(3-cyano-6-methyl-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



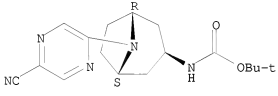
RN 596817-16-2 CAPLUS
CN Carbamic acid, [(3-exo)-8-(6-cyano-3-pyridazinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



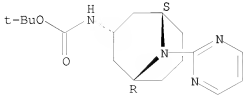
RN 596817-22-0 CAPLUS
CN Carbamic acid, [(3-exo)-8-(5-cyanopyrazinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



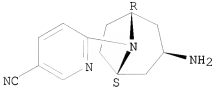
RN 596817-37-7 CAPLUS
CN Carbamic acid, [(3-endo)-9-(2-pyrimidinyl)-9-azabicyclo[3.3.1]non-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



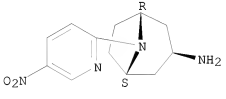
RN 596817-66-2 CAPLUS
CN 3-Pyridinecarbonitrile, 6-[(3-exo)-3-amino-8-azabicyclo[3.2.1]oct-8-yl]- (CA INDEX NAME)

Relative stereochemistry.



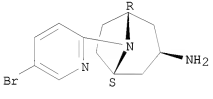
RN 596817-67-3 CAPLUS
CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(5-nitro-2-pyridinyl)-, (3-exo)- (CA INDEX NAME)

Relative stereochemistry.



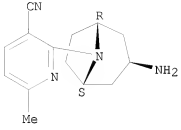
RN 596817-70-8 CAPLUS
CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(5-bromo-2-pyridinyl)-, (3-exo)- (CA INDEX NAME)

Relative stereochemistry.



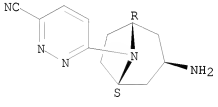
RN 596817-71-9 CAPLUS
CN 3-Pyridinecarbonitrile, 2-[(3-exo)-3-amino-8-azabicyclo[3.2.1]oct-8-yl]-6-methyl- (CA INDEX NAME)

Relative stereochemistry.



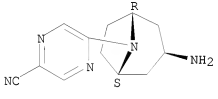

RN 596817-72-0 CAPLUS
CN 3-Pyridazinecarbonitrile, 6-[(3-exo)-3-amino-8-azabicyclo[3.2.1]oct-8-yl]-
(CA INDEX NAME)

Relative stereochemistry.



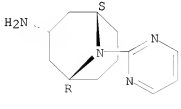

RN 596817-78-6 CAPLUS
CN Pyrazinecarbonitrile, 5-[(3-exo)-3-amino-8-azabicyclo[3.2.1]oct-8-yl]-
(9CI) (CA INDEX NAME)

Relative stereochemistry.




RN 596817-92-4 CAPLUS
CN 9-Azabicyclo[3.3.1]nonan-3-amine, 9-(2-pyrimidinyl)-, (3-endo)- (CA INDEX
NAME)

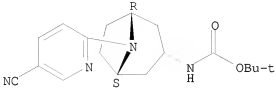
Relative stereochemistry.




RN 637331-09-0 CAPLUS

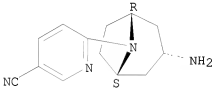
CN Carbamic acid, [(3-endo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.




RN 637331-13-6 CAPLUS
CN 3-Pyridinecarbonitrile, 6-[(3-endo)-3-amino-8-azabicyclo[3.2.1]oct-8-yl]- (CA INDEX NAME)

Relative stereochemistry.

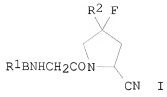


L3 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:719461 CAPLUS
DOCUMENT NUMBER: 139:245893
TITLE: Preparation of aminoacetylpyrrolidinecarbonitriles as inhibitors of DPP-IV
INVENTOR(S): Aranyi, Peter; Balazs, Laszlo; Bata, Imre; Batori, Sandor; Boronkay, Eva; Bovy, Philippe; Kanai, Karoly; Kapui, Zoltan; Susan, Edit; Szabo, Tibor; Nagy, Lajos T.; Urban-Szabo, Katalin; Varga, Marton
PATENT ASSIGNEE(S): Sanofi-Synthelabo, Fr.; et al.
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003074500 | A2 | 20030912 | WO 2003-HU17 | 20030304 |
| WO 2003074500 | A3 | 20031218 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| HU 2002000849 | A2 | 20040830 | HU 2002-849 | 20020306 |
| CA 2475312 | A1 | 20030912 | CA 2003-2475312 | 20030304 |
| AU 2003209514 | A1 | 20030916 | AU 2003-209514 | 20030304 |
| EP 1487807 | A2 | 20041222 | EP 2003-743452 | 20030304 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| BR 2003007960 | A | 20050215 | BR 2003-7960 | 20030304 |
| CN 1639159 | A | 20050713 | CN 2003-805263 | 20030304 |
| JP 2005529078 | T | 20050929 | JP 2003-572969 | 20030304 |
| NZ 535662 | A | 20070531 | NZ 2003-535662 | 20030304 |
| CN 1990486 | A | 20070704 | CN 2006-10164020 | 20030304 |
| TW 250978 | B | 20060311 | TW 2003-92104743 | 20030306 |
| IN 2004KN01079 | A | 20060127 | IN 2004-KN1079 | 20040728 |
| ZA 2004006467 | A | 20050622 | ZA 2004-6467 | 20040813 |
| MX 2004PA08613 | A | 20050608 | MX 2004-PA8613 | 20040906 |
| NO 2004004221 | A | 20041206 | NO 2004-4221 | 20041005 |
| US 2005130981 | A1 | 20050616 | US 2005-507005 | 20050131 |

PRIORITY APPLN. INFO.: HU 2002-849 A 20020306
CN 2003-805263 A3 20030304
WO 2003-HU17 W 20030304

OTHER SOURCE(S): MARPAT 139:245893
GI

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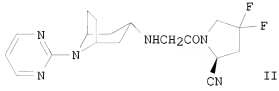


II

AB Title compds. I [R1 = (un)substituted N heteroarom., thienyl, furyl, CH2Ph, tosyl, acyl; B = N heterocyclic; R2 = H, F] were prepared for use as dipeptidyl peptidase IV (DPP-IV) inhibitors with IC50 ≤ 100 nM, useful in the treatment of diabetes. Thus, the title compound II was prepared from 8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl-exo-amine and (2S)-1-chloroacetyl-4,4-difluoro-2-pyrrolidinecarbonitrile, each prepared in several steps.

IT 596816-99-8P 596817-00-4P 596817-03-7P
596817-04-8P 596817-09-3P 596817-10-6P
596817-11-7P 596817-12-8P 596817-13-9P
596817-14-0P 596817-15-1P 596817-16-2P
596817-17-3P 596817-18-4P 596817-19-5P
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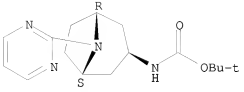
596817-92-4P 599165-27-2P 599165-28-3P
599165-29-4P 599165-31-8P 599165-32-9P
599165-33-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aminoacetylpyrrolidinecarbonitriles as inhibitors of DPP-IV)

RN 596816-99-8 CAPLUS

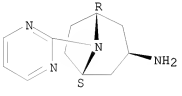
CN Carbamic acid, [(3-exo)-8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



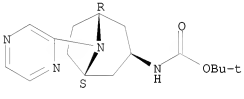
RN 596817-00-4 CAPLUS
CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(2-pyrimidinyl)-, (3-exo)- (CA INDEX NAME)

Relative stereochemistry.



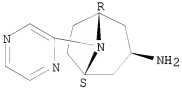
RN 596817-03-7 CAPLUS
CN Carbamic acid, [(3-exo)-8-pyrazinyl-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



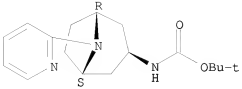
RN 596817-04-8 CAPLUS
CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-pyrazinyl-, (3-exo)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



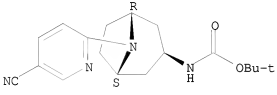
RN 596817-09-3 CAPLUS
CN Carbamic acid, [(3-exo)-8-(2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



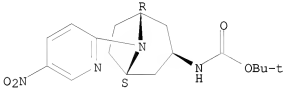
RN 596817-10-6 CAPLUS
CN Carbamic acid, [(3-exo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



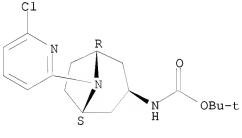
RN 596817-11-7 CAPLUS
CN Carbamic acid, [(3-exo)-8-(5-nitro-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



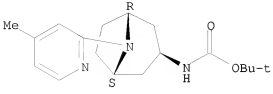
RN 596817-12-8 CAPLUS
CN Carbamic acid, [(3-exo)-8-(6-chloro-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



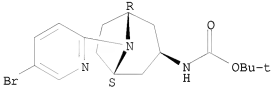
RN 596817-13-9 CAPLUS
CN Carbamic acid, [(3-exo)-8-(4-methyl-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



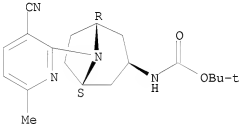
RN 596817-14-0 CAPLUS
CN Carbamic acid, [(3-exo)-8-(5-bromo-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



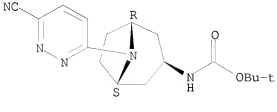
RN 596817-15-1 CAPLUS
CN Carbamic acid, [(3-exo)-8-(3-cyano-6-methyl-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



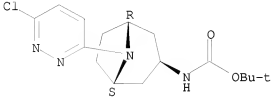
RN 596817-16-2 CAPLUS
CN Carbamic acid, [(3-exo)-8-(6-cyano-3-pyridazinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



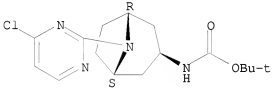
RN 596817-17-3 CAPLUS
CN Carbamic acid, [(3-exo)-8-(6-chloro-3-pyridazinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



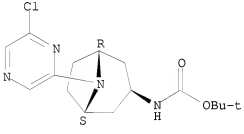
RN 596817-18-4 CAPLUS
CN Carbamic acid, [(3-exo)-8-(4-chloro-2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



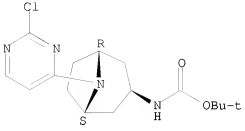
RN 596817-19-5 CAPLUS
CN Carbamic acid, [(3-exo)-8-(6-chloropyrazinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



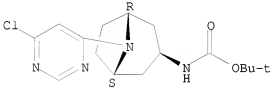
RN 596817-20-8 CAPLUS
CN Carbamic acid, [(3-exo)-8-(2-chloro-4-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



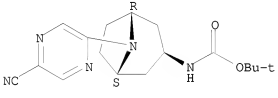
RN 596817-21-9 CAPLUS
CN Carbamic acid, [(3-exo)-8-(6-chloro-4-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



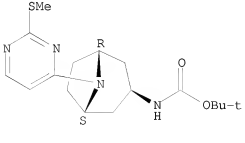
RN 596817-22-0 CAPLUS
CN Carbamic acid, [(3-exo)-8-(5-cyanopyrazinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



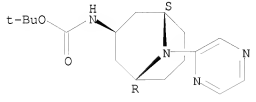
RN 596817-23-1 CAPLUS
CN Carbamic acid, [(3-exo)-8-[2-(methylthio)-4-pyrimidinyl]-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



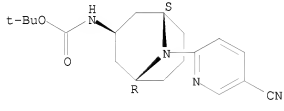
RN 596817-34-4 CAPLUS
CN Carbamic acid, [(3-exo)-9-pyrazinyl-9-azabicyclo[3.3.1]non-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



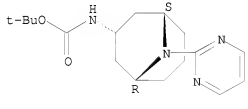
RN 596817-35-5 CAPLUS
CN Carbamic acid, [(3-exo)-9-(5-cyano-2-pyridinyl)-9-azabicyclo[3.3.1]non-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



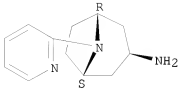
RN 596817-37-7 CAPLUS
CN Carbamic acid, [(3-endo)-9-(2-pyrimidinyl)-9-azabicyclo[3.3.1]non-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



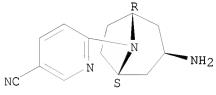
RN 596817-65-1 CAPLUS
CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(2-pyridinyl)-, (3-exo)- (CA INDEX NAME)

Relative stereochemistry.



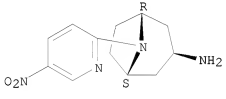
RN 596817-66-2 CAPLUS
CN 3-Pyridinecarbonitrile, 6-[(3-exo)-3-amino-8-azabicyclo[3.2.1]oct-8-yl]- (CA INDEX NAME)

Relative stereochemistry.



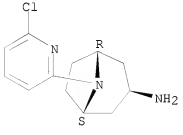
RN 596817-67-3 CAPLUS
CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(5-nitro-2-pyridinyl)-, (3-exo)- (CA INDEX NAME)

Relative stereochemistry.



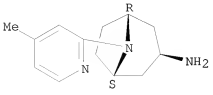
RN 596817-68-4 CAPLUS
CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(6-chloro-2-pyridinyl)-, (3-exo)- (CA INDEX NAME)

Relative stereochemistry.



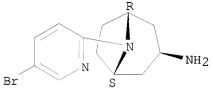
RN 596817-69-5 CAPLUS
CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(4-methyl-2-pyridinyl)-, (3-exo)- (CA INDEX NAME)

Relative stereochemistry.



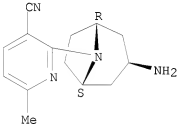

RN 596817-70-8 CAPLUS
CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(5-bromo-2-pyridinyl)-, (3-exo)- (CA INDEX NAME)

Relative stereochemistry.



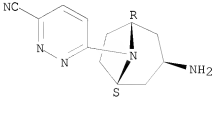

RN 596817-71-9 CAPLUS
CN 3-Pyridinecarbonitrile, 2-[(3-exo)-3-amino-8-azabicyclo[3.2.1]oct-8-yl]-6-methyl- (CA INDEX NAME)

Relative stereochemistry.



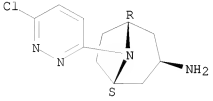

RN 596817-72-0 CAPLUS
CN 3-Pyridazinecarbonitrile, 6-[(3-exo)-3-amino-8-azabicyclo[3.2.1]oct-8-yl]- (CA INDEX NAME)

Relative stereochemistry.



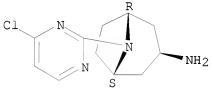
RN 596817-73-1 CAPLUS
CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(6-chloro-3-pyridazinyl)-, (3-exo)-
(CA INDEX NAME)

Relative stereochemistry.



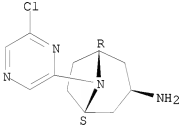

RN 596817-74-2 CAPLUS
CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(4-chloro-2-pyrimidinyl)-, (3-exo)-
(CA INDEX NAME)

Relative stereochemistry.



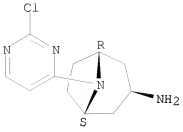

RN 596817-75-3 CAPLUS
CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(6-chloropyrazinyl)-, (3-exo)- (9CI)
(CA INDEX NAME)

Relative stereochemistry.



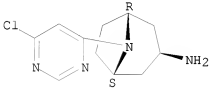

RN 596817-76-4 CAPLUS
CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(2-chloro-4-pyrimidinyl)-, (3-exo)-
(CA INDEX NAME)

Relative stereochemistry.



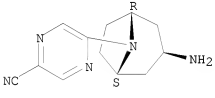
RN 596817-77-5 CAPLUS
CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(6-chloro-4-pyrimidinyl)-, (3-exo)-
(CA INDEX NAME)

Relative stereochemistry.



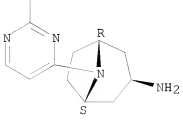
RN 596817-78-6 CAPLUS
CN Pyrazinecarbonitrile, 5-[(3-exo)-3-amino-8-azabicyclo[3.2.1]oct-8-yl]-
(9CI) (CA INDEX NAME)

Relative stereochemistry.



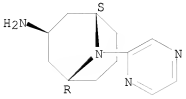
RN 596817-79-7 CAPLUS
CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-[2-(methylthio)-4-pyrimidinyl]-,
(3-exo)- (CA INDEX NAME)

Relative stereochemistry.



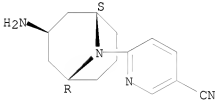
RN 596817-89-9 CAPLUS
CN 9-Azabicyclo[3.3.1]nonan-3-amine, 9-pyrazinyl-, (3-exo)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



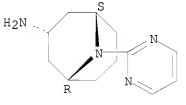
RN 596817-90-2 CAPLUS
CN 3-Pyridinecarbonitrile, 6-[(3-exo)-3-amino-9-azabicyclo[3.3.1]non-9-yl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



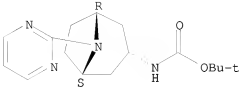
RN 596817-92-4 CAPLUS
CN 9-Azabicyclo[3.3.1]nonan-3-amine, 9-(2-pyrimidinyl)-, (3-endo)- (CA INDEX NAME)

Relative stereochemistry.



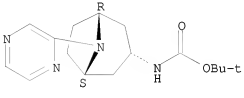
RN 599165-27-2 CAPLUS
CN Carbamic acid, [(3-endo)-8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



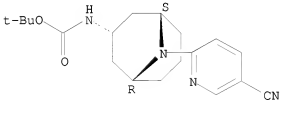
RN 599165-28-3 CAPLUS
CN Carbamic acid, [(3-endo)-8-pyrazinyl-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



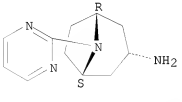
RN 599165-29-4 CAPLUS
CN Carbamic acid, [(3-endo)-9-(5-cyano-2-pyridinyl)-9-azabicyclo[3.3.1]non-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



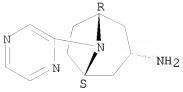
RN 599165-31-8 CAPLUS
CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(2-pyrimidinyl)-, (3-endo)- (CA INDEX NAME)

Relative stereochemistry.



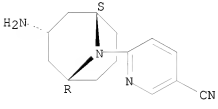
RN 599165-32-9 CAPLUS
CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-pyrazinyl-, (3-endo)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



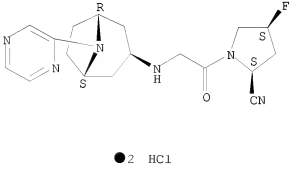
RN 599165-33-0 CAPLUS
CN 3-Pyridinecarbonitrile, 6-[(3-endo)-3-amino-9-azabicyclo[3.3.1]non-9-yl]-
(9CI) (CA INDEX NAME)

Relative stereochemistry.



IT 596816-23-8P 596816-26-1P 596816-27-2P
596816-28-3P 596816-29-4P 596816-30-7P
596816-31-8P 596816-32-9P 596816-33-0P
596816-34-1P 596816-35-2P 596816-36-3P
596816-37-4P 596816-38-5P 596816-39-6P
596816-40-9P 596816-41-0P 596816-51-2P
596816-52-3P 596816-53-4P 596816-56-7P
596818-14-3P 599165-24-9P 599165-25-0P
599165-36-3P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminoacetylpyrrolidinecarbonitriles as inhibitors of DPP-IV)
RN 596816-23-8 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[(3-exo)-8-pyrazinyl-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

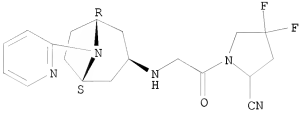
Absolute stereochemistry.



●2 HCl

RN 596816-26-1 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-exo)-8-(2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)

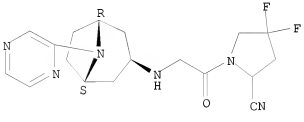
Relative stereochemistry.



●2 HCl

RN 596816-27-2 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-exo)-8-pyrazinyl-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)

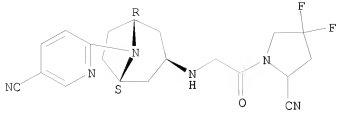
Relative stereochemistry.



●2 HCl

RN 596816-28-3 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

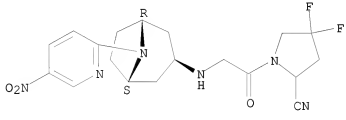
Relative stereochemistry.



●2 HCl

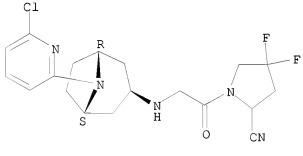
RN 596816-29-4 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-exo)-8-(5-nitro-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 596816-30-7 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(6-chloro-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

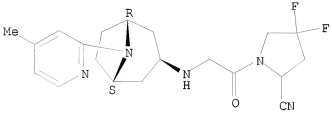


●2 HCl

RN 596816-31-8 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-exo)-8-(4-methyl-2-

pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, trihydrochloride
(9CI) (CA INDEX NAME)

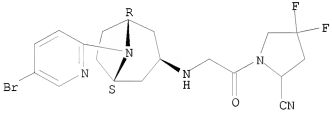
Relative stereochemistry.




●3 HCl

RN 596816-32-9 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(5-bromo-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride
(9CI) (CA INDEX NAME)

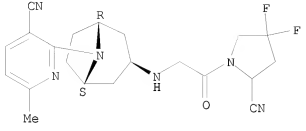
Relative stereochemistry.




●2 HCl

RN 596816-33-0 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(3-cyano-6-methyl-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride
(9CI) (CA INDEX NAME)

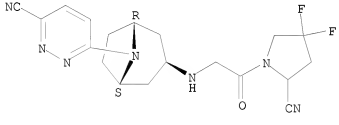
Relative stereochemistry.



●2 HCl

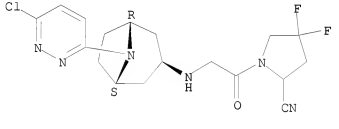
RN 596816-34-1 CAPLUS
CN 3-Pyridazinecarbonitrile, 6-[(3-exo)-3-[[2-(2-cyano-4,4-difluoro-1-pyrrolidinyl)-2-oxoethyl]amino]-8-azabicyclo[3.2.1]oct-8-yl]- (CA INDEX NAME)

Relative stereochemistry.



RN 596816-35-2 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(6-chloro-3-pyridazinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

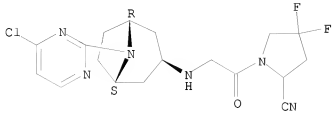


●2 HCl

RN 596816-36-3 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(4-chloro-2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride

(9CI) (CA INDEX NAME)

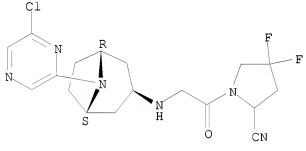
Relative stereochemistry.



●2 HCl

RN 596816-37-4 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(6-chloropyrazinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

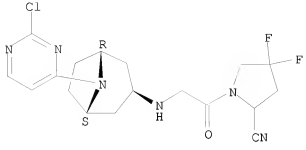
Relative stereochemistry.



●2 HCl

RN 596816-38-5 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(2-chloro-4-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

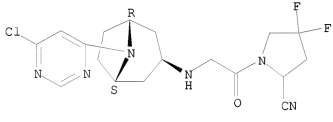
Relative stereochemistry.



●2 HCl

RN 596816-39-6 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(6-chloro-4-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

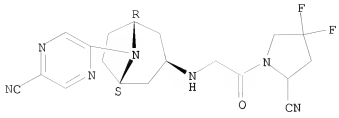
Relative stereochemistry.



●2 HCl

RN 596816-40-9 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(5-cyanopyrazinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, hydrochloride (2:3) (9CI) (CA INDEX NAME)

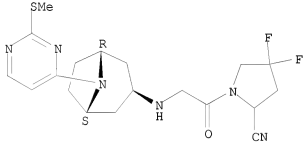
Relative stereochemistry.



●3/2 HCl

RN 596816-41-0 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-exo)-8-[2-(methylthio)-4-pyrimidinyl]-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)

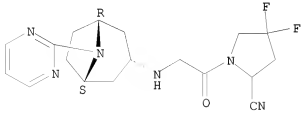
Relative stereochemistry.



●2 HCl

RN 596816-51-2 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-endo)-8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]- (9CI) (CA INDEX NAME)

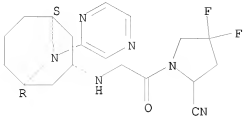
Relative stereochemistry.



RN 596816-52-3 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-exo)-9-pyrazinyl-9-azabicyclo[3.3.1]non-3-yl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX

NAME)

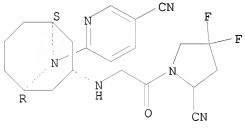
Relative stereochemistry.



●2 HCl

RN 596816-53-4 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-9-(5-cyano-2-pyridinyl)-9-azabicyclo[3.3.1]non-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

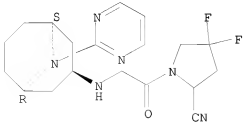
Relative stereochemistry.



●2 HCl

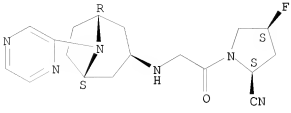
RN 596816-56-7 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-endo)-9-(2-pyrimidinyl)-9-azabicyclo[3.3.1]non-3-yl]amino]acetyl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



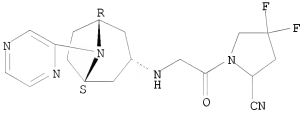
RN 596818-14-3 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[(3-exo)-8-pyrazinyl-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 599165-24-9 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-endo)-8-pyrazinyl-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, trihydrochloride (9CI) (CA INDEX NAME)

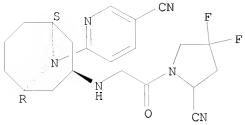
Relative stereochemistry.



●3 HCl

RN 599165-25-0 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-endo)-9-(5-cyano-2-pyridinyl)-9-azabicyclo[3.3.1]non-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

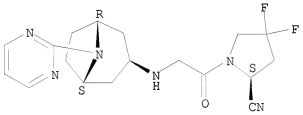
Relative stereochemistry.



●2 HCl

RN 599165-36-3 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-exo)-8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

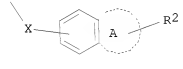
Absolute stereochemistry.



L3 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:964330 CAPLUS
DOCUMENT NUMBER: 138:39295
TITLE: Preparation of heterocyclic compounds as Rho-kinase inhibitors
INVENTOR(S): Imazaki, Naonori; Kitano, Masafumi; Ohashi, Naohito; Matsui, Kazuki
PATENT ASSIGNEE(S): Sumitomo Pharmaceuticals Company, Limited, Japan
SOURCE: PCT Int. Appl., 425 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002100833 | A1 | 20021219 | WO 2002-JP5609 | 20020606 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2002306284 | A1 | 20021223 | AU 2002-306284 | 20020606 |
| EP 1403255 | A1 | 20040331 | EP 2002-733352 | 20020606 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| US 2004138286 | A1 | 20040715 | US 2003-480526 | 20031212 |
| US 7199147 | B2 | 20070403 | | |
| PRIORITY APPLN. INFO.: | | | JP 2001-176826 | A 20010612 |
| | | | JP 2001-398992 | A 20011228 |
| | | | WO 2002-JP5609 | W 20020606 |

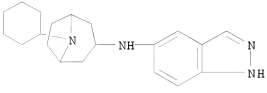
OTHER SOURCE(S): MARPAT 138:39295
GI




I

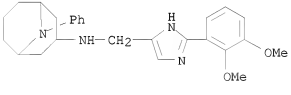
AB The title compds. I [wherein one to four groups represented by the general formula R1-X are present and may be the same or different from each other; A is a saturated or unsatd. five-membered heterocycle; X is a single bond, N(R3), O, S, or the like; R1 is hydrogen, halogeno, nitro, carboxyl, substituted or unsubstituted alkyl, or the like; R2 is hydrogen, halogeno, nitro, carboxyl, substituted or unsubstituted alkyl, or the like; and R3 is hydrogen, substituted or unsubstituted alkyl, or the like] are prepared N-(1-Benzyl-4-piperidinyl)-1H-indazole-5-amine dihydrochloride monohydrate in vitro showed IC50 of 0.4 μL/mL against Rho-kinase.

IT 478837-97-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclic compds. as Rho-kinase inhibitors)
RN 478837-97-7 CAPLUS
CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-cyclohexyl-N-1H-indazol-5-yl- (CA INDEX NAME)

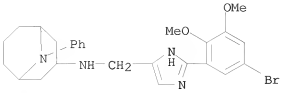



REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:827020 CAPLUS
DOCUMENT NUMBER: 136:294764
TITLE: Synthesis of 2-(2,3-dimethoxyphenyl)-4-(aminomethyl)imidazole analogues and their binding affinities for dopamine D2 and D3 receptors
AUTHOR(S): Huang, Yunsheng; Luedtke, Robert R.; Freeman, Rebekah A.; Wu, Li; Mach, Robert H.
CORPORATE SOURCE: Department of Radiology-PET Center, Wake Forest University School of Medicine, Winston-Salem, NC, 27157, USA
SOURCE: Bioorganic & Medicinal Chemistry (2001), 9(12), 3113-3122
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:294764
AB A series of 2-(2,3-dimethoxyphenyl)-4-(aminomethyl)imidazole derivs. was prepared and their affinity for dopamine D2 and D3 receptors was measured using in vitro binding assays. Several oxadiazole analogs were also prepared and tested for their affinity for dopamine D2 and D3 receptors. The results of receptor binding studies indicated that the incorporation of an imidazole moiety between the Ph ring and the basic nitrogen did not significantly increase the selectivity for dopamine D3 receptors, whereas the incorporation of an oxadiazole at the same region resulted in a total loss of affinity for both dopamine receptor subtype binding sites. The most selective compound in this series is 6,7-dimethoxy-2-[[2-(2,3-dimethoxyphenyl)-1H-imidazol-4-yl]methyl]-1,2,3,4-tetrahydroisoquinoline, which has a D3 receptor affinity of 21 nM and a 7-fold selectivity for D3 vs. D2 receptors. The binding affinity for σ1 and σ2 receptors was also measured, and the results showed that several analogs were selective σ1 receptor ligands.
IT 407610-27-9P 407610-28-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and dopamine D2 and D3 receptor affinity of 2-(2,3-dimethoxyphenyl)-1H-imidazole-4-methanamine derivs.)
RN 407610-27-9 CAPLUS
CN 9-Azabicyclo[3.3.1]nonan-3-amine, N-[[2-(2,3-dimethoxyphenyl)-1H-imidazol-4-yl]methyl]-9-phenyl- (9CI) (CA INDEX NAME)




RN 407610-28-0 CAPLUS
CN 9-Azabicyclo[3.3.1]nonan-3-amine, N-[[2-(5-bromo-2,3-dimethoxyphenyl)-1H-imidazol-4-yl]methyl]-9-phenyl- (9CI) (CA INDEX NAME)




REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:229244 CAPLUS
DOCUMENT NUMBER: 135:13871
TITLE: Synthesis and structure-activity relationships of naphthamides as dopamine D3 receptor ligands
AUTHOR(S): Huang, Yunsheng; Luedtke, Robert R.; Freeman, Rebekah A.; Wu, Li; Mach, Robert H.
CORPORATE SOURCE: Department of Radiology-PET Center and Department of Physiology Pharmacology, Wake Forest University School of Medicine, Winston-Salem, NC, 27157, USA
SOURCE: Journal of Medicinal Chemistry (2001), 44(11), 1815-1826
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:13871

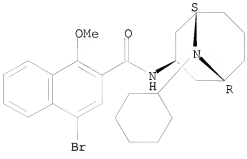
AB A series of naphthamides were synthesized, and the affinities of these compds. were determined for dopamine D2 and D3 receptors using radioligand binding techniques. The naphthamide compds. that were prepared include N-(1-alkylpiperidin-4-yl)-4-bromo-1-methoxy-2-naphthamides (1-6), (S)-N-(1-alkylpyrrolidin-3-yl)-4-bromo-1-methoxy-2-naphthamides (7-12), (R)-N-(1-alkylpyrrolidin-3-yl)-4-bromo-1-methoxy-2-naphthamides (13-18), (S)-N-(1-alkyl-2-pyrrolidinylmethyl)-4-bromo-1-methoxy-2-naphthamides (19-25), (R)-N-(1-alkyl-2-pyrrolidinylmethyl)-4-bromo-1-methoxy-2-naphthamides (26-31), and N-(9-alkyl-9-azabicyclo[3.3.1]nonan-3β-yl)-4-bromo-1-methoxy-2-naphthamides (32, 33). The results of in vitro radioligand binding studies indicated that the majority of the naphthamide analogs bound with high affinity at both the D2 and D3 dopamine receptor subtypes and most of the compds. demonstrated some selectivity for the dopamine D3 dopamine receptor subtype. These results demonstrated that both the structure of the central amine moiety (piperidine, pyrrolidine, and 9-azabicyclo[3.3.1]nonane) ring and the N-(alkyl) substitution on the amine significantly effects the binding affinity at D2 and D3 dopamine receptors. The bulkiness of the N-(1-alkyl) substituent was found to (a) have no effect on pharmacol. selectivity, (b) increase the affinity at D3 receptors, or (c) decrease the affinity at D2 receptors. The most potent analog in this series was (S)-N-(1-cycloheptylpyrrolidin-3-yl)-4-bromo-1-methoxy-2-naphthamide (10), which had equilibrium dissociation (Ki) values of 1.8 and 0.2 nM for D2 and D3 receptors, resp. The most selective analog was (R)-N-(1-cycloheptyl-2-pyrrolidinylmethyl)-4-bromo-1-methoxy-2-naphthamide (30), which had Ki values of 62.8 and 2.4 nM for D2 and D3 receptors, resp. Radioligand binding results for σ receptors indicated that the structure of the amine moiety and the N-(1-alkyl) substitutions also significantly influence the affinity and selectivity of these compds. at the σ1 and σ2 sigma receptor subtypes. The two naphthamides containing a 9-azabicyclo[3.3.1]nonan-3β-yl central ring were found to be selective for σ2 receptors.

IT 342876-79-3P
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(design and SAR of naphthamides as dopamine D3 receptor ligands)

RN 342876-79-3 CAPLUS
CN 2-Naphthalenecarboxamide, 4-bromo-N-[(3-exo)-9-cyclohexyl-9-

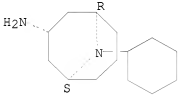
azabicyclo[3.3.1]non-3-yl]-1-methoxy- (CA INDEX NAME)

Relative stereochemistry.




IT 342876-83-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(design and SAR of naphthamides as dopamine D3 receptor ligands)
RN 342876-83-9 CAPLUS
CN 9-Azabicyclo[3.3.1]nonan-3-amine, 9-cyclohexyl-, (3-exo)- (CA INDEX NAME)

Relative stereochemistry.

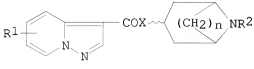



REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1993:101950 CAPLUS
DOCUMENT NUMBER: 118:101950
TITLE: Preparation of pyrazolo[1,5-a]pyridine derivatives as serotonin 3 (5-HT3) antagonists
INVENTOR(S): Ito, Yasuo; Kato, Hideo; Yasuda, Shingo; Iwasaki, Nobuhiko; Nishino, Hiroyuki
PATENT ASSIGNEE(S): Hokuriku Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 04257591 | A | 19920911 | JP 1991-37776 | 19910208 |
| PRIORITY APPLN. INFO.: | | | JP 1991-37776 | 19910208 |

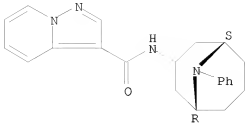
OTHER SOURCE(S): MARPAT 118:101950
GI



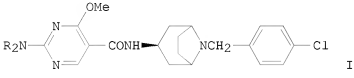

I

AB The title derivs. I (R1 = H, lower alkyl; R2 = H, PhCH2, lower alkyl; X = NH, O; n = 2, 3) or their pharmaceutically acceptable salts are prepared as 5-HT3 antagonists (no data). Chlorination of 1.00 g pyrazolo[1,5-a]pyridine-3-carboxylic acid in CH2Cl2 gave pyrazolo[1,5-a]pyridine-3-carbonyl chloride, which in CH2Cl2 was added dropwise into a mixture of 0.95 g exo-8-methyl-8-azabicyclo[3.3.1]octan-3-amine and Et3N in CH2Cl2 under ice cooling, then stirred at room temperature for 1.5 h to give 0.88 g exo-N-(8-methyl-8-azabicyclo[3.2.1]oct-3-yl)pyrazolo[1,5-a]pyridine-3-carboxamide.
IT 145663-01-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as 5-HT3 antagonist)
RN 145663-01-0 CAPLUS
CN Pyrazolo[1,5-a]pyridine-3-carboxamide, N-(9-phenyl-9-azabicyclo[3.3.1]non-3-yl)-, endo- (9CI) (CA INDEX NAME)

Relative stereochemistry.


N
N
H
N
O
S
N
Ph
R

L3 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1984:510862 CAPLUS
DOCUMENT NUMBER: 101:110862
ORIGINAL REFERENCE NO.: 101:16933a,16936a
TITLE: Studies on the neuroleptic benzamides. III. Synthesis and antidopaminergic properties of new 3-nortropane derivatives
AUTHOR(S): Dostert, Philippe; Imbert, Thierry; Langlois, Michel; Bucher, Bernard; Mocquet, Gisele
CORPORATE SOURCE: Cent. Rech., Rueil-Malmaison, 92500, Fr.
SOURCE: European Journal of Medicinal Chemistry (1984), 19(2), 105-10
CODEN: EJMCA5; ISSN: 0009-4374
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 101:110862
GI




I

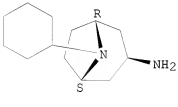
AB Pyrimidinecarboxamides were prepared from 4-alkoxypyrimidine-5-carboxylic acids and 3-aminonortropane derivs. and were tested for their potential antipsychotic activity. I (R = H, Me) had pharmacol. activity equivalent to that of haloperidol but had lower toxicity and lower potency to induce catalepsy. Some aspects of structure-activity relationships are discussed.

IT 76272-54-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(acylation of, with aminomethoxypyrimidinecarboxylic acid)

RN 76272-54-3 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-cyclohexyl-, exo- (9CI) (CA INDEX NAME)

Relative stereochemistry.

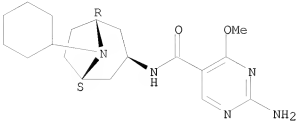



IT 91595-99-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn and antidopaminergic activity of)

RN 91595-99-2 CAPLUS

CN 5-Pyrimidinecarboxamide, 2-amino-N-(8-cyclohexyl-8-azabicyclo[3.2.1]oct-3-yl)-4-methoxy-, exo- (9CI) (CA INDEX NAME)

Relative stereochemistry.



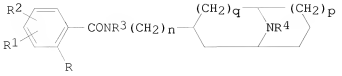
L3 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1981:65477 CAPLUS
DOCUMENT NUMBER: 94:65477
ORIGINAL REFERENCE NO.: 94:10669a,10672a
TITLE: Azabicycloalkyl derivatives and pharmaceutical compositions containing them
INVENTOR(S): Hadley, Michael Stewart; King, Francis David
PATENT ASSIGNEE(S): Beecham Group Ltd., UK
SOURCE: Eur. Pat. Appl., 63 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 13138 | A1 | 19800709 | EP 1979-302978 | 19791220 |
| EP 13138 | B1 | 19831207 | | |
| R: AT, BE, CH, DE, FR, GB, IT, NL, SE | | | | |
| EP 81054 | A2 | 19830615 | EP 1982-109116 | 19791220 |
| EP 81054 | A3 | 19830824 | | |
| EP 81054 | B1 | 19861217 | | |
| R: AT, BE, CH, DE, FR, GB, IT, NL, SE | | | | |
| AT 24320 | T | 19870115 | AT 1982-109116 | 19791220 |
| EP 220339 | A1 | 19870506 | EP 1985-115575 | 19791220 |
| EP 220339 | B1 | 19891108 | | |
| R: BE, CH, DE, FR, GB, IT, NL, SE | | | | |
| DK 7905539 | A | 19800815 | DK 1979-5539 | 19791221 |
| JP 55092384 | A | 19800712 | JP 1979-170199 | 19791226 |
| US 4273778 | A | 19810616 | US 1979-107413 | 19791226 |
| AU 7954255 | A | 19800703 | AU 1979-54255 | 19791228 |
| AU 527837 | B2 | 19830324 | | |
| ES 487379 | A1 | 19801201 | ES 1979-487379 | 19791228 |
| ZA 7907054 | A | 19801231 | ZA 1979-7054 | 19791228 |
| CA 1218062 | A1 | 19870217 | CA 1979-342845 | 19791231 |
| US 4336259 | A | 19820622 | US 1980-200768 | 19801027 |
| US 4544660 | A | 19851001 | US 1981-271990 | 19810609 |
| US 4599420 | A | 19860708 | US 1983-469681 | 19830225 |
| CA 1220473 | A2 | 19870414 | CA 1984-446870 | 19840206 |
| US 4705858 | A | 19871110 | US 1986-824458 | 19860131 |
| JP 02072178 | A | 19900312 | JP 1989-112779 | 19890501 |
| JP 03075548 | B | 19911202 | | |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| GB 1978-50380 | A | 19781230 |
| GB 1979-9262 | A | 19790315 |
| GB 1979-27831 | A | 19790809 |
| EP 1979-302978 | A | 19791220 |
| EP 1982-109116 | A | 19791220 |
| US 1979-107413 | A3 | 19791226 |
| CA 1979-342845 | A3 | 19791231 |
| US 1981-271990 | A3 | 19810609 |
| US 1983-469681 | A3 | 19830225 |

OTHER SOURCE(S): MARPAT 94:65477
GI




I

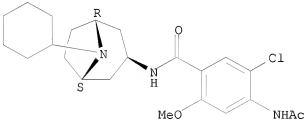
AB Azabicycloalkanes I (R = alkoxy; R1, R2 = H, halogen, CF3, acyl, acylamino, NH2, optionally substituted CONH2, SO2NH2, alkylsulfonyl, NO2; R3 = H, alkyl; R4 = optionally substituted alkyl; n, p, q = 0-2) were prepared Thus I [R = OMe, R1 = 4-NHAc (II), R2 = 5-Cl, R3 = H, R4 = CH2Ph, n = p = 0, q = 1] was obtained as a mixture of 3'α- and 3'β-isomers by acylating 3-amino-8-benzylnortropane (III) and was deacylated to II (R1 = 4-NH2). III was obtained by LiAlH4 reduction of 8-benzyl-3-nortropanone oxime. II (R1 = 4-NH2) inhibited apomorphine-induced stereotype behavior at ≤10 mg/kg s.c. in rats and was antiemetic at 0.0025 mg/kg s.c. in dogs.

IT 76272-92-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and deacetylation of)

RN 76272-92-9 CAPLUS

CN Benzamide, 4-(acetylamino)-5-chloro-N-(8-cyclohexyl-8-azabicyclo[3.2.1]oct-3-yl)-2-methoxy-, exo- (9CI) (CA INDEX NAME)

Relative stereochemistry.

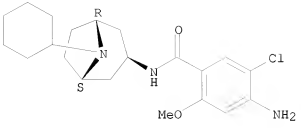



IT 76272-91-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and dopamine antagonist and antiemetic activity of)

RN 76272-91-8 CAPLUS

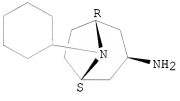
CN Benzamide, 4-amino-5-chloro-N-(8-cyclohexyl-8-azabicyclo[3.2.1]oct-3-yl)-2-methoxy-, exo- (9CI) (CA INDEX NAME)

Relative stereochemistry.




IT 76272-54-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with methoxybenzoyl chloride derivative)
RN 76272-54-3 CAPLUS
CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-cyclohexyl-, exo- (9CI) (CA INDEX NAME)

Relative stereochemistry.



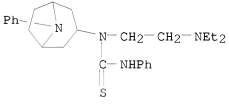
L3 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1961:82268 CAPLUS
DOCUMENT NUMBER: 55:82268
ORIGINAL REFERENCE NO.: 55:15609d-e
TITLE: State of transforming deoxyribonucleic acid (DNA) during the first phase of bacterial transformation
AUTHOR(S): Taylor, Harriett Ephrussi
CORPORATE SOURCE: Lab. genetique physiol., Gif-sur-Yvette, Fr.
SOURCE: Comptes Rendus des Seances de la Societe de Biologie et de Ses Filiales (1960), 154, 1951-5
CODEN: CRSBAW; ISSN: 0037-9026
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB Expts. with pneumococci seemed to indicate that at the stage of fixation of added transforming DNA the latter is firmly bound to a protein of the receptor cell, and that it retains its high mol. weight until liberation within the cell by growth processes.

IT 123935-68-2P, Urea, 1-(2-diethylaminoethyl)-3-phenyl-1-(8-phenyl-3-nortropanyl)-2-thio-
RL: PREP (Preparation)
(preparation of)

RN 123935-68-2 CAPLUS

CN Urea, 1-(2-diethylaminoethyl)-3-phenyl-1-(8-phenyl-3-nortropanyl)-2-thio- (6CI) (CA INDEX NAME)



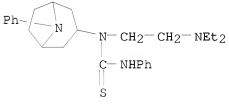
L3 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1961:82267 CAPLUS
DOCUMENT NUMBER: 55:82267
ORIGINAL REFERENCE NO.: 55:15609c-d
TITLE: Action of lysozyme on Haemophilus pertussis
AUTHOR(S): Dumazert, C.; Ghiglione, C.
SOURCE: Bulletin de la Societe de Pharmacie de Marseille (1960), 9, 145-59,161-71
CODEN: BSPMAC; ISSN: 0560-5237
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB Action of lysozyme on bacterial suspensions of H. pertussis resulted in the isolation of a glucoside fraction and a protein fraction. The glucoside contains glucose, galactose, and an unidentified N base. The protein has not been fully characterized. Immunological studies on the glucoside fraction indicate properties similar to a hapten isolated from Pneumococcus.

IT 123935-68-2P, Urea, 1-(2-diethylaminoethyl)-3-phenyl-1-(8-phenyl-3-nortropanyl)-2-thio-
RL: PREP (Preparation)
(preparation of)

RN 123935-68-2 CAPLUS

CN Urea, 1-(2-diethylaminoethyl)-3-phenyl-1-(8-phenyl-3-nortropanyl)-2-thio- (6CI) (CA INDEX NAME)



L3 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1959:2191 CAPLUS
DOCUMENT NUMBER: 53:2191
ORIGINAL REFERENCE NO.: 53:430h-i,431a-i,432a-i
TITLE: Tertiary amino substituted 1,5-iminocycloalkanes
INVENTOR(S): Archer, Sydney
PATENT ASSIGNEE(S): Sterling Drug Inc.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2845427 | | 19580729 | US 1955-483808 | 19550124 |

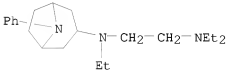
AB N-Substituted 1,5-iminocycloalkanes (I) attached at the 3-position through an O, S, or N atom to a tertiary amino alkyl group, which are useful for the reduction of hypertension (the salts and quaternary derivs. are even more active), are prepared by treating a 3-oxo derivative of I with a tertiary amino alkylamine and reducing the resulting imine by condensing the 3-alkali metal sulfide or oxide derivative of I with a tertiary amino alkyl halide and (or) by condensing 3-halo derivative of I with the alkali metal salt of a tertiary amino alkyl mercaptan or hydroxide. 3-Tropolone (30 g.), 24 g. Et2N(CH2)2NH2, 1.2 g. PtO2, and 50 ml. EtOH was shaken 1 hr. under 50 lb. H, filtered, and the filtrate distilled to give 33.2 g. 3-(2-diethylaminoethylamino)-tropane (II), b0.5 111-15°; tri-HCl salt, m. 267-71°; picrate, m. 163.5-6°; dimethiodide, m. 269°; dimethobromide, m. 289-90°. II (59 g.) was cooled to solid CO2 temperature, 54 ml. 100% HCO2H and 24.6 ml. 36% H2CO added, the mixture heated on the steam bath 16 hrs., cooled and made basic, extracted with Et2O, and the product distilled to yield 42.5 g. 3-[(2-diethylaminoethyl)methylamino]tropane, b0.8-1 120-3°, n25D 1.4871; tri-HBr salt, m. above 140°; dimethiodide, m. 242-4°; dimethobromide, m. 245-7°; diethiodide, m. 237-8°. Similarly the following 3-substituted derivs. of tropane were prepared (side chain, b.p./mm., and salts with their m.p. given): Me2N(CH2)2NH, 101.5-3°/0.5 (n25D 1.4880); Me2N(CH2)2NMe, 104-7°/1.2 (n25D 1.4900-9), di-MeI 238-41°; C5H10N(CH2)3NH, 141-50°/0.5; C5H10N(CH2)3NMe, 141-8°/0.2 (n25D 1.5057), di-MeI 222-3°, tri-MeI 207-14°; C5H10N(CH2)2NH, 132-3°/0.5, tri-HCl 275-7°, di-MeI 293°; C5H10N(CH2)2NMe, 118.5-26°/0.07, tri-HBr 220-4.5°, di-MeI 259-66°, di-EtI 215-19°; C4H4N(CH2)3NH, 140-4°/0.05; C4H4N(CH2)3NMe, 129-31°/0.2 (n25D 1.5031-40), di-MeI 226-8°; C4H4N(CH2)2NH, 130-5°/0.5, di-MeI 290-3°; C4H4N(CH2)2NMe, 122-4°/0.3 (n25D 1.5055-60), di-MeI 205-20°; C4H4N(CH2)4NH, 142-8°/0.3 (n25D 1.5038-41); C4H4N(CH2)4NMe, 138-41°/0.2 (n52D 1.5029); OC4H8N(CH2)2NH, 133-5°/0.4 (n25D 1.5066), tri-HCl 245-9.5°, di-MeI 264-5°; OC4H8N(CH2)2NMe, 124-30°/0.1 (n25D 1.5079-83), tri-HBr 252-4°, di-MeI 218-20°; Me2N(CH2)3NH, 112-14°/1.7 (n25D 1.4990), picrate 230°; Me2N(CH2)3NMe, 106-12°/0.5 (n25D 1.4885-8), picrate 231°; Et2N(CH2)3NH, 120-5°/0.1 (n25D 1.4862); Et2N(CH2)3NMe, 120-30/0.1 (n25D 1.4870), di-MeI 222-7°; PhMeN(CH2)2NH (III), 167-73°/0.1; PhEtN(CH2)2NH (IV), 174-7°/0.6, MeI 226-8°; p-MeC6H4NMe(CH2)2NH, 164-73°/0.3 (n23.5D 1.5532);

p-MeOC6H4NMe(CH2)2NH, 179-83°/0.5 (n24D 1.5560); NH(CH2)2NH (bis compound), 178-81°/0.6; and NMe(CH2)2NMe (bis compound), 192-200°/1.5, di-MeI 273-4°. II (3.8 g.) and 2.2 g. PhNCS heated in MeOH gave 3.7 g. 1-(2-diethylaminoethyl)-1-(3-tropanyl)-3-phenylthiourea (V), m. 170.5-2°. The following derivs. of II were prepared (group replacing the H of the secondary amine, b.p./mm., or m.p., and certain salts with their m.p. given): MeCH:CHNHCS, 97-100°; EtNHCS, 122-4°; 4-EtOC6H4NHCS, 160-1°; Ac (VI), 142-4°/0.09 (n25D 1.4980), picrate 198-200°; EtCO (VII), 160°/0.5 (n25D 1.4940-5), picrate 173-6°; and PrCO (VIII), 162-6°/0.7 (n28D 1.4935), picrate 194-6°. VI, VII, and VIII were reduced with LiAlH4 in Et2O to the following N-substituted derivs. of II (substituent, b.p./mm., n28D, and salts given): Et, 142°/2, 1.4845, di-MeI 230-1°, di-EtI 226°; Pr, 119-26°/0.1, 1.4835, picrate 223°, di-MeI 203-9°; and Bu, 125-30°/0.1, 1.4839, picrate 208-10°. Other 3-substituted tropane derivs. that were prepared are (side chain, b.p. m/m., and salts given): C4H4N(CH2)2N(CHO), 166-72°/0.9 (n24D 1.5131); PhEtN(CH2)2N(CHO), 200-7°/0.1-0.2; PhEtN(CH2)2NMe, 182-7°/15 (n24D 1.5518), di MeI 240-2°; p-MeC6H4NMe(CH2)2N(CHO), 95-7°; p - MeC6H4NMe(CH2)2NMe, 174-6°/0.5 (n24D 1.5508-10), HCl 168°, tri-MeI 215°; p-MeOC6H4NMe(CH2)2N(CHO), 112-14°; p-MeOC6H4NMe(CH2)2NMe (IX), 162-6°/0.1 (n25D 1.5518), picrate 205-7°, di-MeI 195-8°. Formic acid (26.5 ml.), 500 ml. H2O, and 29 g. III followed by 10 ml. 37% H2CO was heated 15 hrs. on the steam bath to give 1-methyl-4-(3-tropanyl)-1,2,4,5-tetrahydro-1,4-benzodiazepine (X), b0.6 155-65°; di-MeI salt (XI), m. 264-7°; di-EtI salt, m. 208-10°. X was methylated in the 7-position with H2CO and HCO2H, b0.2 163°; picrate, m. 230-1°; methiodide, m. 274-6°. XI subjected to a Hofmann degradation gave 1-[(2-dimethylaminobenzyl)vinylamino]-3-dimethylamino-5-cycloheptene; dipicrate, m. 193-4°. IV, H2CO, and HCO2H gave the 1-Et homolog of X, b0.5 174-8° (di-MeI salt, m. 269-71°; MeI salt, m. 235-8°; di-MeBr salt, m. 262-2.5°; di-EtBr salt, m. 253-4°), and IX under these conditions gave the 7-methoxy derivative of X, b0.1 180-5°; picrate, m. 239-40°. III heated with 98% HCO2H gave 3-[2-(phenylmethylaminoethyl)formylamino]tropane, b0.5 216-22°, which was reduced with LiAlH4 to the N-Me derivative, b0.6 160-5°; dimethiodide, m. 255°; dimethobromide, m. 258°. Tropine (60 g.) in 50 ml. MePh was added to 9.2 g. Na in 100 ml. MePh, the mixture refluxed 4 hrs. and 42.8 g. Me2N(CH2)2Cl added, the mixture refluxed 3 hrs., aqueous MeOH added, and distilled to give 17.3 g. 3-(2-dimethylaminoethoxy)tropane, b0.9 85-5.5°, n25D 1.4836; diperchlorate, m. 243-6°; dimethiodide, m. 314-15°; diethiodide, m. 269-75°. Similarly, the following 3-substituted tropanes were prepared (side chain, b.p./mm., and salts and their m.p. given): Et2N(CH2)2O, 101°/0.07 (n25D 1.4758), di-MeI 301-2°; C5H10N(CH2)2O, 106-9°/0.07, di-MeI 305°; C5H10N(CH2)3O, 115°/0.1, di-MeI above 305°; C4H4N(CH2)2O, 134°/2.8 (n25D 1.4932), di-MeI 313-14°; Et2N(CH2)3O(CH2)3O, 94-6°/0.2, di-MeI 300°. Pseudotropine, Na, and Et2(CH2)2Cl in C6H6 gave 3-(2-diethylaminoethoxy)pseudotropane, b0.25, 109-12°, n25D 1.4775; dimethiodide, m. 307-8°. Tropanone (69.5 g.), 63.8 g. Et2N(CH2)2NH2, and 500 mg. ZnCl2 in MePh was heated 64 hrs. using an H2O separator to yield 92.2 g. 3-(2-diethylaminoethylimino)tropane (XII), b0.6 117-31°. XII was reduced by Na and EtOH to a mixture of 3-(2-diethylaminoethylamino)tropane and pseudotropane. The mixture of

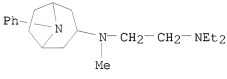
isomers and PhNCS gave V and the isomeric pseudotropane, m. 138-9.5°. By this procedure pseudopelletierine (XIII) and C5H10N(CH2)2NH2 yielded 3-[2-(1-piperidyl)ethylimino]-9-methylgranatanine, bl 164-76°, n25D 1.5235, which was reduced by Na in Me2CH(CH2)3OH to a mixture of isomers of the corresponding amine which was treated with PhNCS in MeOH to yield a mixture of isomers of the thiourea (XIV), m. 174.5-6°, (XV) m. 173-4.5° (AcOEt). XIV (7.3 g.), MeOH, and 25 ml. 4N HCl in EtOH was evaporated, the residue heated 30 min. at 100°, dissolved in EtOH, and the solution cooled to yield 3-[2-(1-piperidyl)ethylamino]-9-methylgranatanine; tri-HCl salt (XVI), m. 285-7°. XV treated in this manner gave an isomer of XVI, m. 276°. Similarly, XIII with the appropriate amine gave the following 3-substituted derivs. of 9-methylgranatanine (side chain, b.p./mm., and salts with their m.p. given; when isomers were obtained, both m.p.'s given): C4H4N(CH2)2NH, 144-6°/1 (n24D 1.5252); C4H4N(CH2)2NH, 155-7°/2 (n25D 1.5102), di-MeI 278°; C4H4N(CH2)2(PhNHCS)N, 173-4°; Et2N(CH2)2NH, 131-9°/0.7 (n25D 1.5050); Et2N(CH2)2NH, 128-30°/0.6 (n25D 1.4920), tri-HCl 278° and 185°, di-MeI 277-9°; Et2N(CH2)2(PhNHCS)N, 189-91° and 135-6°. Concentrated HCl (0.13 ml.) was added to 160 g. 2,5-diethoxytetrahydrofuran in 150 ml. H2O, the suspension stirred 2 hrs. at 48-50° and cooled, 202 g. (EtO2CCH2)2CO, 100 ml. H2O, 107 g. PhCH2NH2, and 83 ml. HCl added, the mixture stirred overnight, 250 ml. HCl added, heated while 270 ml. H2O was distilled, the residue filtered, the filtrate made basic with NaOH, 500 g. K2CO3 added, and the mixture extracted with Et2O to yield 102 g. 8-benzyltropanone (XVII), b0.4 134-7°, n25D 1.5526. XVII yielded 3-(2-diethylaminoethylamino)-8-benzylnortropane, b0.25 161-8°, n25D 1.5235; tri-HCl salt, m. 264-6°; dimethiodide, m. 255-7°; phenylthiourea derivative, m. 138-9°. The following 8-benzylnortropane derivs. are described (side chain and phenyl substituents, b.p./mm. or m.p., and salts given): 4'-MeO, 3-oxo, 179-84°/0.1 (n25D 1.5538), HCl 203-4°; 4'-MeO, 3-Et2N(CH2)2HN, tri-HCl 277-8°, di-MeI 229-30°; 2',3'-di-MeO, 3-oxo, 178-99°/0.5, HCl 201-2°; 2'-3'-di-MeO, 3-Et2N(CH2)2HN, tri-HCl 234-7°, di-MeI 226-8°; 3,'4'-OCH2O, 3-oxo, tri-HCl 223-3.5°;3',4'-OCH2O,3-Et2N(CH2)2HN, tri-HCl 275-6°, di-MeI 234-7°; 3',4'-OCH2O 3-Et2N(CH2)2(PhNHCS)N, 148-9°; 4'-Cl, 3-oxo, 168-80°/0.8; 4'-Cl, 3-Et2N(CH2)2HN, di-MeI 232-4°, di-MeBr 228-30.5°; 2'-Cl, 3-Et2N(CH2)2(PhNHCS)N, 124-6°; 2'-Cl, 3-C4H4N(CH2)2HN, tri-HCl 253°, di-MeI 218-20°; 2'-MeO, 3-oxo, 174-81°/0.2-0.5 (n25D 1.5061-5), HCl 177-8°; 2'-MeO, 3-Et2N(CH2)2HN, tri-HCl 248-51°, di-MeI 218.5-21.5°; 2',4'-di-Cl, 3-oxo, 185-7°/1.5, tri-HCl 216°; and 2,4-di-Cl, 3-Et2N(CH2)2NH, di-MeI 237-9°. 8-Phenylnortropanone, m. 107-9°, was prepared by the method used for XIII and reaction with Et2N(CH2)2NH2, PtO2, and H gave 3-(2-diethylaminoethylamino)-8-phenylnortropane (XVIII), b0.2 153-68°, which with PhNCS gave the thiourea derivative, m. 161-3°, and with Ac2O yielded N-Ac derivative of XVIII, b0.2 183-98°, n25D 1.5470, which was reduced to the N-Et derivative of XVIII, b0.9 180-4°, n30D 1.5370. PhEtN(CH2)2NH2 (35 g.), 32 g. XIII, 1 g. ZnCl2, and 200 ml. MePh gave 3-(2-phenylmethylaminoethylaminoethylamino)-9-methylgranatanine, b0.2-0.9 160-84°, n30D 1.5575, from which the following N-substituted derivs. were prepared (b.p./mm. and salts with their m.p. given): HCO, 190-220°/0.7; Me, 161-6°/0.15, picrate 191-4°, di-MeI 225-7°; Ac, 200-14°/0.2; and Et, 162-7°/0.1, picrate 203-5°.

IT 102457-13-6P, Nortropane, 3-[(2-diethylaminoethyl)ethylamino]-8-phenyl- 102463-23-0P, Nortropane, 3-[(2-diethylaminoethyl)methylamino]-8-phenyl- 102709-02-4P, Nortropane, 3-[(2-diethylaminoethyl)amino]-8-phenyl- 110147-72-3P , Nortropane, 3-[N-(2-diethylaminoethyl)acetamido]-8-phenyl- 123935-68-2P, Urea, 1-(2-diethylaminoethyl)-3-phenyl-1-(8-phenyl-3-nortropanyl)-2-thio-
RL: PREP (Preparation)
(preparation of)

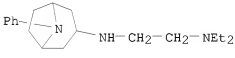
RN 102457-13-6 CAPLUS
CN Nortropane, 3-[(2-diethylaminoethyl)ethylamino]-8-phenyl- (6CI) (CA INDEX NAME)



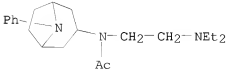
RN 102463-23-0 CAPLUS
CN Nortropane, 3-[(2-diethylaminoethyl)methylamino]-8-phenyl- (6CI) (CA INDEX NAME)



RN 102709-02-4 CAPLUS
CN Nortropane, 3-[(2-diethylaminoethyl)amino]-8-phenyl- (6CI) (CA INDEX NAME)

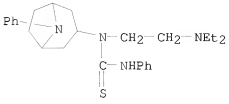


RN 110147-72-3 CAPLUS
CN Nortropane, 3-[N-(2-diethylaminoethyl)acetamido]-8-phenyl- (6CI) (CA INDEX NAME)



RN 123935-68-2 CAPLUS

CN Urea, 1-(2-diethylaminoethyl)-3-phenyl-1-(8-phenyl-3-nortropanyl)-2-thio- (6CI) (CA INDEX NAME)



L3 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1958:6906 CAPLUS
DOCUMENT NUMBER: 52:6906
ORIGINAL REFERENCE NO.: 52:1292a-i,1293a-b
TITLE: 3-(Monocarbocyclic aryl-(lower alkyl)amino-1,5-iminocycloalkanes
INVENTOR(S): Archer, Sydney
PATENT ASSIGNEE(S): Sterling Drug Inc.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2798874 | | 19570709 | US 1955-502745 | 19550420 |

GI For diagram(s), see printed CA Issue.

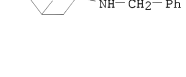
AB Compds. of the general formula RN.CH.CH2.(CH2)m.CH.CH2.CH(NR'CnH2nAr).CH2 and their salts, where R is lower alkyl, monocarbocyclic aryl, or aryl lower alkyl, R' is H or lower alkyl, m is 1-2, n is 1-6, and Ar is a monocarbocyclic aryl group, are useful in reducing hypertension and exhibit ganglionic blocking action in cats and dogs. They are prepared by reaction of a 3-tropinone (via the Robinson synthesis) and ArCnH2nNH2 under hydrogenation conditions. E.g., 45 g. 3-tropinone (I), 32 g. PhCH2NH2, 1.0 g. PtO2, and 150 ml. EtOH are shaken 4 hrs. at 55° with H at 50 lb. per sq. in. One mole H is taken up. After filtration, the mixture is distilled and redistd. to obtain 34.8 g. 3-benzylaminotropane (II), b0.8 140-2°, n25D 1.5450; picrate, m. 160-1°. II (29.6 g.) is cooled to 20° and 28.2 cc. 98% HCO2H added portionwise followed by 13 cc. 36% HCHO solution, the mixture warmed to room temperature, heated 17 hrs. on a steam bath, poured into ice H2O, made basic with 35% NaOH solution, extracted with ether, dried over K2CO3, and distilled to get 21.2 g. 3-(benzylmethylamino)tropane (III), b0.3 135-8°, n25D 1.5416; picrate, m. 230-2° (from HCONMe2); methiodide, m. 233.0-7.5° (decomposition). I (42 g.), 52.5 cc. 5.82N MeNH2 in MeOH, 1.5 g. PtO2, and 100 ml. MeOH treated similarly yield 38.3 g. 3-methylaminotropane (IV), b23 109-10°, n25D 1.4934. When 15.2 g. IV, 12.6 g. PhCH2Cl, and 13.8 g. K2CO3 in 100 cc. PhMe are heated 4 hrs. under reflux and 10% K2CO3 solution then added, three layers are formed. The bottom (aqueous) layer is discarded; the top (PhMe) layer is distilled to dryness, the residue dissolved in ether, filtered, and the filtrate distilled to get 5.6 g. III, b0.8 130-6°. The middle layer is taken up in CHCl3, washed with H2O, and the CHCl3 distilled, ether added to an EtOH solution of the residue, and the solid (3.7 g.) separated and recrystd. from EtOH-ether to obtain the 8-benzochloride of III (V), m. 224.0-5.5° (decomposition); 8-(4-nitrobenzobromide) (VI), m. 220-3° (decomposition); 8-(4-chlorobenzochloride) (VII), m. 226-8° (decomposition); 8-(3,4-dichlorobenzochloride) (VIII), m. 232-5° (decomposition); 8-(p-methoxybenzochloride); 8-(p-methylbenzochloride). 3-(4-Chlorobenzylamino)tropane (IX), b0.2 135-53°; picrate, m. 185-7°. 3-(2-Phenylethylamino)-, 3-(3-phenylpropylamino)-, and 3-(2-phenylpropylamino)tropane are prepared by analogous methods. IX is heated with 1 molar equivalent PhNCS to obtain the phenylthiureide, m. 130-2°. Replacement of I in the synthesis of IX with pseudopelletierine gives 3-(4-chlorobenzylamino)-9-methylgranatanine. IX (18.0 g.), 15 ml. 98% HCO2H, and 6.85 ml. 37% HCHO solution yield 12.4 g.

3-[(4-chlorobenzyl)methylamino]tropane (X), b0.3 140°; 8-methiodide (XI), m. 255-6° (decomposition); 8-methobromide, m. 261-3° (decomposition); 8-(4-nitrobenzobromide), m. 210-12° (decomposition). X, b0.1-0.2 144-6°, n25D 1.5483, and its 8-(4-chlorobenzochloride) (XII), m. 202.5-205° (decomposition), are prepared by the method used for III and V. The 8-(3,4-dichlorobenzochloride) of XII, m. 200-3° (decomposition); 8-(2-hydroxyethobromide), m. 219-21°. A mixture of 50 g. 4-Et2NC6H4CH2NH2 and 200 ml. 12% NH3 in MeOH is hydrogenated (Raney Ni) 3 hrs. at 21-2° at an initial pressure of 890 lbs. per sq. in., filtered, distilled, and redistd. to obtain 23.2 g. 4-diethylaminobenzylamine (XIII), b0.1 122-8°, n25D 1.5592. Hydrogenation of 19.0 g. I, 23.2 g. XIII, and 1 g. PtO2 in 200 ml. absolute EtOH as before, solution of the crude product in absolute EtOH, and addition of excess alc. HCl give 21.5 g. 3-(4-diethylaminobenzylamino)tropane trihydrochloride dihydrate, m. 195° (decomposition); picrate of free base, m. 185° (decomposition). The phenylthiureide m. 145-7°; 8-methiodide (XIV), m. 240-5° (decomposition); 8-(4-chlorobenzochloride) (XV), m. 208-11° (decomposition); 8-(3,4-dichlorobenzochloride), m. 200-3° (decomposition); 8-(4-nitrobenzobromide), m. 189-91°. 3-(Benzylacetylamino)tropane is prepared by treating II with Ac2O followed by hydrolysis; reduction with LiAlH4 yields 3(benzylethylamino)tropane. A solution of 36.2 g. 2,5-diethoxytetrahydrofuran in 240 cc. H2O containing 0.6 ml. concentrated H2SO4 is warmed 15 min. on a steam bath, cooled, and added to a solution of 97 g. CO(CH2CO2H)2, 146 NaOAc.3H2O, and 27 PhNH2 in 3.5 l. H2O. After standing overnight, the solid is collected, dissolved in one 1.5% aqueous HCl at 60°, cooled, made alkaline with NH3, and the product recrystd. from dilute MeOH to obtain 11.4 g. 8-phenylnortropanone (XVI), m. 107-9°; hydrogenation of a mixture of XVI, PhCH2NH2, and PtO2 in EtOH gives 3-benzylamino-8-phenylnortropanone. V, VI, VII, VIII, XI, and XII are 60, 54, 74, 128, 30, and 100% as effective, resp., as hexamethylenebis(trimethylammonium bromide) in blockade of the sympathetic ganglia when measured by the carotid occlusion test in dogs. X, XIV, and XV are similarly 35, 26, and 210% as effective, resp., in cats.

IT 102552-20-5P, Nortropane, 3-benzylamino-8-phenyl-
RL: PREP (Preparation)
(preparation of)

RN 102552-20-5 CAPLUS

CN Nortropane, 3-benzylamino-8-phenyl- (6CI) (CA INDEX NAME)



L3 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1957:86038 CAPLUS
DOCUMENT NUMBER: 51:86038
ORIGINAL REFERENCE NO.: 51:15607c-i,15608a-i,15609a-h
TITLE: Tertiary amino-substituted compounds of the tropane and granatanine series
PATENT ASSIGNEE(S): Sterling Drug Inc.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| GB 762256 | | 19561128 | GB | |

AB Tertiary amino substituted tropanes, granatanines, and their salts are prepared 3-Tropanone (30 g.), 24 g. 2-diethylaminoethylamine, 1.2 g. PtO2, and 50 ml. EtOH is shaken in 50 lb./sq. in. H 2.5 hrs., the product filtered, the filtrate concentrated, and distilled to give 33.2 g. 3-(2-diethylaminoethylamino)tropane, b5 111-15°; picrate, m. 163.5-6° (from aqueous EtOH); trihydrochloride monohydrate, m. 267-71° (from 95% EtOH, MeOH); bismethiodide, m. 269° (from dilute MeOH) (decomposition). To 59 g. 3-[(2-diethylaminoethyl)amino]tropane cooled to -40° is added 54 ml. 100% HCO2H followed by 24.6 ml. 36% HCHO, the mixture heated to 100° 16 hrs., treated with 35% NaOH, extracted with Et2O, and then distilled to yield 42.5 g. 3-[(2-diethylaminoethyl)methylamino]tropane, b-1.0 120-3°, nD25 1.4871. Similarly the following compds. are prepared: 3-[(2-diethylaminoethyl)amino]tropane bismethobromide, m. 289-90° (from MeOH) (decomposition); 3-[(2-diethylaminoethyl) methylamino]tropane trihydrobromide, m. 140° (from MeOH); 3-[(2-dimethylaminoethyl)amino]tropane, b0.5 101.5-3°, nD25 1.4880; 3-[(2-dimethylaminoethyl)methylamino]tropane, b1.2 104-7°, nD25 1.4900-9, m. 238-41° (decomposition); 3-[3-(1-piperidyl)propylamino]tropane, b0.2 141.8-°, nD25 1.5057; 3-{[3-(1-piperidyl)propyl]methylamino}tropane bisethiodide, m. 222-33°; 3-{[3-(1-piperidyl)propyl]methylamino}tropane trismethiodide, m. 207-14°; 3-[2-(1-piperidyl)ethylamino]tropane, b0.5 132-3°; 3-[2-(1-piperidyl)ethylamino]tropane trihydrochloride, m. 275-7°; 3-[2-(1-piperidyl)ethylamino]tropane bis-methiodide, m. 293°; 3-{[2-(1-piperidyl)ethyl]methylamino}tropane, b0.07 118.5-26°; 3-{[2-(1-piperidyl)ethyl]methylamino}tropane trihydrobromide, m. 220-4.5°; 3-{[2-(1-piperidyl)ethyl]methylamino}tropane bismethiodide, m. 259-60°; 3-{[2-(1-piperidyl)ethyl] methylamino}tropane bisethiodide, m. 215-19°; 3-[3-(1-pyrrolidyl)propylamino]tropane, b0.05 140-4°; 3-{[3-(1-pyrrolidyl)propyl]methylamino}tropane, b0.2 129-31°, nD25 1.5031-40; 3-{[3-(1-pyrrolidyl)propyl]methylamino}tropane bismethiodide, m. 226-8°; 3-[2-(1-pyrrolidyl)ethylamino]tropane, b0.5 130-5°; 3-[2-(1-pyrrolidyl)ethylamino]tropane bismethiodide, m. 290-3° (decomposition); 3-{[2-(1-pyrrolidyl)ethyl]methylamino}tropane, b0.3 122-4°, nD25 1.5055-60; 3-{[2-(1-pyrrolidyl)ethyl]methylamino}tropane bismethiodide, m. 205-20°; 3-[4-(1-pyrrolidyl)butylamino]tropane, b0.3 142-8°, nD25 1.5038-41; 3-{[4-(1-pyrrolidyl)butyl]methylamino}tropane, b0.2 138-40°, nD25.5 1.5029; 3-[2-(4-morpholinylethylamino]tropane, b0.4 133-5°, nD25 1.5066;

3-[2-(4-morpholinylethylamino]tropane trihydrochloride, m. 245-9° (with decomposition); 3-[2-(4-morpholinyl)ethylamino]tropane bismethiodide, m. 264.5-5° (decomposition); 3-{[2-(4-morpholinyl)ethyl]methylamino}tropane , b0.1 124-30°, nD25 1.5079-83; 3-{[2-(4-morpholinyl)ethyl] methylamino}tropane trihydrobromide, m. 252-4° (decomposition); 3-{[2-(4-morpholinyl)ethyl]methylamino}tropane bismethiodide, m. 218-20°; 3-(3-dimethylaminopropylamino) tropane, b1.7 112-14°, nD24 1.4990 (tripicrate, m. 230°); 3-[(3-dimethylaminopropyl)methylamino]tropane, b0.5 106-12°, nD26 1.4885-8 [picrate, m. 231° (decomposition)]; 3-(3-diethylaminopropylamino)tropane, b0.1 120-5°, nD25 1.4862 [picrate,m. 212° (decomposition)]; 3-[(3-diethylaminopropyl)methylamino] tropane, b0.1 120-3°, nD25 1.4870; 3-[(3-diethylaminopropyl)methylamino]tropane bismethiodide, m. 222-7°. Tropine (60 g.), 150 ml. PhMe, and 9.2 g. Na is refluxed 4 hrs., then 3 more hrs. with 42.8 g. 2-dimethylaminoethyl chloride in 50 ml. PhMe, aqueous MeOH added to the cooled product, and the organic layer separated, concentrated, and distilled to yield 17.3 g. 3-(2-diethylaminoethoxy)tropane, b0.9 85-0.5°, nD25 1.4836; bisperchlorate, m. 243-6° (from aqueous AcOH); bismethiodide, m. 314-5° (from MeOH) (decomposition). Similarly, the following compds. are prepared: 3-(2-diethylaminoethoxy)tropane, b0.07 101°, nD25 1.4758; 3-(2-diethylaminoethoxy)tropane bismethiodide, m. 301-2° (decomposition); 3-[2-(1-piperidyl)ethoxy]tropane, b0.07 106-9°; 3-[2-[1-piperidyl)ethoxy]tropane bismethiodide, m. above 305°; 3-[3-(1-piperidyl)propoxy]tropane, b0.1 115°; 3-[3-(1-piperidyl)propoxy]tropane bismethiodide, m. above 305°; 3-[2-(1-pyrrolidyl)ethoxy]tropane, b2.8 134°, nD25 1.4932; 3-[2-(1-pyrrolidyl)ethoxy]tropane bismethiodide, m. 313-4°; 3-(2-diethylaminoethoxy)pseudotropane, b0.25 109-12°, nD25 1.4775; 3-(2-diethylaminoethoxy)pseudotropane bismethiodide, m. 307-8° (decomposition); 3-(3-diethylaminopropoxy)tropane, b0.2 94-6°; 3-(3-diethylaminopropoxy)tropane bismethiodide, m. 300° (decomposition). 3-(2-Diethylaminoethylmercapto)tropane can be prepared by heating 3-bromotropane with 3-diethylaminoethylmercaptan in NaOH solution 1-Methyl-4-(3-tropanyl)-1,2,4,5-tetrahydro-1,4-benzodiazepine bismethiodide, m. 264-7° (from H2O) (decomposition). Similarly the following compds. are prepared: 3-(2-phenylmethylaminoethylamino)tropane, b0.1 167-73°; 1-methyl-4-(3-tropanyl)-1,2,4,5-tetrahydro-1,4-benzodiazepine, b0.3 170-2°; 3-(2-phenylethylaminoethylamino)tropane, b0.6 174-7°; 3-(2-phenylethylaminoethylamino)tropane 8-methiodide, m. 226-8° (decomposition); 1-ethyl-4-(3-tropanyl)-1,2,4,5-tetrahydro-1,4-benzodiazepine, b0.5 174-8°; 1-ethyl-4-(3-tropanyl)-1,2,4,5-tetrahydro-1,4-benzodiazepine bismethiodide, m. 269-71°; 1-ethyl-4-(3-tropanyl)-1,2,4,5-tetrahydro-1,4-benzodiazepine 8-methiodide, m. 235-8°; 1-ethyl-4-(3-tropanyl)-1,2,4,5-tetrahydro-1,4-benzodiazepine bismethobromide, m. 262-2.5° (decomposition). 2,5-Diethoxytetrahydrofuran (160 g.), 150 ml. H2O, and 0.13 ml. concentrated HCl stirred at 48-50° 2 hrs., cooled to 25°, 202 g. di-Et acetonedicarboxylate followed by 100 ml. H2O and 107 g. PhCH2NH2.HCl added, the mixture stirred overnight, treated with 250 ml. HCl, and heated to 103° to remove H2O, the residue filtered off, the filtrate made basic with 250 ml. 35% NaOH, 500 g. K2CO3 added, and extracted 3 times with Et2O gave 102 g. 8-benzylnortropanone, b0.4 134-7, nD25 1.5562. Similarly are prepared: 3-(2-diethylaminoethylamino)-8-benzylnortropane, b0.25 161-8°, nD25 1.5235; 3-(2-diethylaminoethylamino)-8-

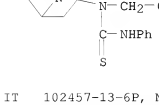
benzylnortropane trihydrochloride, m. 264-6° (decomposition); 3-(2-diethylaminoethylamino)-8-benzylnortropane bismethiodide, m. 255-7°; 3-(2-diethylaminoethylamino)-8-(4-methoxybenzyl) nortropane; 3-(2-diethylaminoethylamino)-8-(4-methoxybenzyl)nortropane trihydrochloride, m. 277-8° (decomposition); 3-(2-diethylaminoethylamino)-8-(4-methoxybenzyl)nortropane bismethiodide, m. 229-30°; 3-(2-diethylaminoethylamino)-8-(2,3-dimethoxybenzyl)nortropane; 3-(2-diethylaminoethylamino)-8-(2,3-dimethoxybenzyl)nortropane trihydrochloride, m. 234-7°; 3-(2-diethylaminoethylamino)-8-(2,3-dimethoxybenzyl)nortropane bismethiodide, m. 226-8°; 3-(2-diethylaminoethylamino)-8-(3,4-methylenedioxybenzyl) nortropane; 3-(2-diethylaminoethylamino)-8-(3,4-methylenedioxybenzyl)nortropane trihydrochloride, m. 275-6° (decomposition); 3-(2-diethylaminoethylamino)-8-(3,4-methylenedioxybenzyl)tropane bismethiodide, m. 234-7°; 3-(2-diethylaminoethylamino)-8-(4-chlorobenzyl)nortropane; 3-(2-diethylaminoethylamino)-8-(4-chlorobenzyl)nortropane trihydrochloride, m. 273-5°; 3-(2-diethylaminoethylamino)-8-(2-chlorobenzyl)nortropane; 3-(2-diethylaminoethylamino)-8-(2-chlorobenzyl)nortropane bismethiodide, m. 232-4°; 3-(2-diethylaminoethylamino)-8-(2-methoxybenzyl)nortropane trihydrochloride, m. 248-51°; 3-(2-diethylaminoethylamino)-8-(2-methoxybenzyl)nortropane bismethiodide, m. 218.5-21.5°; 3-(2-diethylaminoethylamino)-8-phenylnortropane; 3-(2-diethylaminoethyl)methylamino-8-phenylnortropane. Hydrated pseudopelletierine (29.8 g.), 26 g. 2-(1-piperidyl)ethylamine, 600 mg. ZnCl2, and 150 ml. C6H5CH3 refluxed 64 hrs. using a separator to collect the H2O formed, the product cooled, washed with 50 ml. saturated K2CO3 solution, and the aqueous layer extracted with 4 50-ml. portions of C6H6 yielded 27.8 g. 3-2-(1-piperidyl)ethylimino-9-methylgranatanine (II), bl 164-76°, nD25 1.5235. To 27.8 g. II in 40 g. 4-methyl-2-pentanol is added slowly 9.2 g. Na in 200 ml. PhMe, the mixture refluxed 0.5 hr., 30 ml. H2O added, cooled, the aqueous layer saturated with K2CO3, extracted with 3 100-ml. portions of PhMe, the PhMe layers concentrated, dissolved in 50 ml. MeOH, 15 g. phenyl isothiocyanate stirred in, and the precipitate (34.4 g.) filtered off and recrystd. from AcOEt. By fractional precipitation from MeOH 2 isomers of 1-2 (1-piperidyl)ethyl-1-3-(9-methyl)granatanyl-3-phenylthiourea, isomer A, m. 174.5-6° (prisms from AcOEt), and isomer B, 173-4.5° (needles) are obtained. Also prepared were: 3-[2-(1-piperidyl)ethylamino]-9-methylgranatanine trihydrochloride (from isomer A), m. 285-7° (decomposition); 3-[2-(1-piperidyl) ethylamino]-9-methylgranatanine trihydrochloride (from isomer B), m. 276° (decomposition); 1-(2-diethylaminoethyl)-1-(3-tropanyl)-3-phenylthiourea, m. 170.5-2°; 3-(2-diethylaminoethylimino)tropane, b0.6 117-31°; 3-(2-diethylaminoethylamino)tropane; 1-(2-diethylaminoethyl)-1-(3-pseudotropanyl)-3-phenylthiourea, m. 138-9.5°; 3-(2-diethylaminoethylamino)pseudotropane trihydrochloride, m. 276° (decomposition); 3-(2-diethylaminoethylamino)pseudotropane bismethiodide, m. 279-81° (MeOH); 3-[2-(1-pyrrolidyl)ethylamino]-9-methylgranatanine, b2 155-7°, nD25 1.5102; 1-[2-(1-pyrrolidyl) ethyl]-1-[3-(9-methyl) granatanyl]-3-phenylthiourea, m. 173-4°; 3-[2-(1-pyrrolidyl)ethylamino]-9-methylgranatanine bismethiodide, m. 278° (decomposition); 3-(2-diethylaminoethylamino)-9-methylgranatanine, b0.6 128-30°, nD25 1.4920; 1-(2-diethylaminoethyl)-1-(9-

methylgranatanyl)-3-phenylthiourea, isomer B, m. 188-90°; 1-(2-diethylaminoethyl)-1-(9-methylgranatanyl)-3-phenylthiourea, isomer A, m. 135-6°; 3-(2-diethylaminoethylamino)-9-methylgranatanine trihydrochloride, isomer A, m. 278° (decomposition) [trihydrochloride of isomer B, m. 185°; bismethiodide of isomer A, m. 277-9° (decomposition)];
1-(2-diethylaminoethyl)-1-{3-[8-(2-chlorobenzyl)nortropanyl]}-3-phenylthiourea, m. 124-6°; 1-(2-diethylaminoethyl)-1-[3-(8-phenyl)nortropanyl]-3-phenylthiourea, m. 161-3°.
3-(2-Diethylaminoethylamino)tropane (4.0 g.) treated with 1.7 ml. allyl isothiocyanate yielded 3.6 g. 1-(2-diethylaminoethyl)-1-(3-tropanyl)-3-allylthiourea, m. 97-100°. Similarly the following compds. are prepared: 1-(2-diethylaminoethyl)-1-(3-tropanyl)-3-ethylthiourea, m. 122-4°; 1-(2-diethylaminoethyl)-1-(3-tropanyl)-3-(4-ethoxyphenyl)thiourea, m. 160-1°; 1-(2-diethylaminoethyl)-1-[3-(8-benzyl)nortropanyl]-3-phenylthiourea, m. 138-9°;
1-(2-diethylaminoethyl)-1-{3[8-(3,4-methylenedioxybenzyl)]nortropanyl}-3-phenylthiourea, m. 148-9°; 3-[(2-diethylaminoethyl)acetylamino]tropane, b0.09 142-4°, nD25 1.4980 (picrate, m. 190-200°) (from EtOH); 3-[(2-diethylaminoethyl)ethylamino]tropane, b2 142°, nD25 1.4845 (bismethiodide, m. 230-1°) (decomposition); 3-[(2-diethylaminoethyl)ethylamino]tropane bismethiodide, m. 226° (decomposition); 3-[(2-diethylaminoethyl)propionylamino]tropane, b0.5 160°, nD28 1.4940-5 (picrate, m. 173-6°) (from aqueous HCONMe2); 3-[(2-diethylaminoethyl)propylamino]tropane, b0.1 119-26°, nD28 1.4835 [picrate, m. 223° (decomposition); bismethiodide, m. 203-9° (decomposition)]; 3-[(2-diethylaminoethyl)butyrylamino]tropane, b0.7 162-6°, nD25 1.4935 (picrate, m. 194-6°);
3-[(2-diethylaminoethyl)butylamino]tropane, b0.1 125-30°, nD25 1.4839 [picrate, m. 208-10° (decomposition)]; 3-[(2-diethylaminoethyl)acetylamino]-8-phenylnortropane, b0.2 183-98°, nD28 1.5470; 3-[(2-diethylaminoethyl)ethylamino]-8-phenylnortropane, b0.9 180-4°, nD30 1.5370; 3-[(2-phenylethylaminoethyl)formylamino]tropane, b0.1-0.2 200-7°; 3-{[2-(1-pyrrolidyl)ethyl]formylamino}tropane, b0.9 166-72°, nD25 1.5131 (picrate, m. 192-4°);
3-[2-phenylethylaminoethyl)methylamino]tropane, b1.6 182-7°, nD24 1.5518.

IT 123935-68-2
(Derived from data in the 6th Collective Formula Index (1957-1961))

RN 123935-68-2 CAPLUS

CN Urea, 1-(2-diethylaminoethyl)-3-phenyl-1-(8-phenyl-3-nortropanyl)-2-thio-(6CI) (CA INDEX NAME)

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RL: PREP (Preparation)
(preparation of)
RN 102457-13-6 CAPLUS
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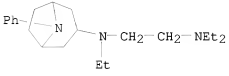

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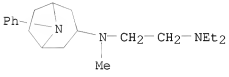

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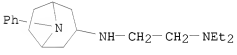

RN 110147-72-3 CAPLUS
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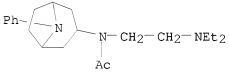


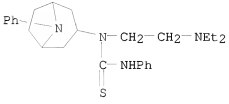
L3 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1957:86037 CAPLUS
DOCUMENT NUMBER: 51:86037
ORIGINAL REFERENCE NO.: 51:15606g-i,15607a-c
TITLE: Heterocyclic alcohol diammonio esters
PATENT ASSIGNEE(S): Cutter Laboratories, Inc.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| GB 770581 | | 19570320 | GB 1955-8626 | 19550324 |

AB Esters containing two quaternary nitrogens, a trialkyl N being on the acid moiety and a heterocyclic N on the alcohol moiety are useful as hypotensor agents. Thus, to make 2-(1-ethylpiperidinium)ethyl 3-(trimethylammonium)propionate diiodide (I), 10.0 g. 1-ethyl-1-(2-hydroxyethyl)piperidinium iodide (II) was first acylated 1 hr. with 26 g. I(CH2)2COCl (III) on a steam bath. This product was washed with Et2O, MeOH and then Et2O to yield a residue which was dissolved in an MeOH-dioxane (10 ml.:25 ml.) and mixed with 2.1 g. Me3N in 16 ml. dioxane. After 3 days, 10.6 g. I, m. 169-71° (from MeOH), separated Directions are given for similar reactions to yield the following 2-(substituted-ethyl)-3-(trimethylammonium)propionate diiodides (substituent on C-2 of ethyl, yield and m.p., crystallization solvent given): 1-methylpiperidinium, 52%, 170-1°, MeOH-Et2O (IV); 1-methylpyrrolidinium, 81%, 190°, IV; 4-methylmorpholinium, 61%, 188-90°, MeOH. An alternative procedure was represented by refluxing 10 g. 2-(4-methyl-1-piperidyl)-2-propyl 3-(dimethylamino)propionate (V), in 500 ml. Me2CO 1 hr. with 20 g. MeI. Upon cooling, the mixture yielded 16.3 g. 2-(1,4-dimethylpiperidinium)-2-propyl 3-(trimethylammonium)propionate diiodide (VA), m. 170-2° (from wet Me2CO). II was prepared in 60% yield by refluxing 24 hrs. 13.5 g. 2-iodoethanol in 50 ml. MeOH with 9.0 g. 1-ethylpiperidine. The oily II which separated on cooling slowly solidified. Crystallization of this solid from Me2CO-MeOH (100 ml.:50 ml.) yielded 10.3 g. II, m. 240°. 1-(2-hydroxyethyl)-1-methylpiperidinium iodide, m. 235-8°, was similarly prepared in 93% yield. Equimolar quantities of 4-methylpiperidine and propylene oxide, when refluxed 4.5 hrs. and distilled, yielded 80% 1-(4-methyl-1-piperidyl)-2-propanol (VI), b. 210-12°. VI was slowly added to 1 mole acrylyl chloride in C6H6 and this mixture then refluxed 2.5 hrs. The C6H6 solution, after washing with cold saturated NaCl solution and excess Na2CO3 solution, yielded 69% 2-(4-methyl-1-piperidyl)-2-propyl acrylate (VII), b2.5 85°. When 1 mole gaseous Me2NH was passed into cold VII and this mixture held 17 days at room temperature (sealed tube), distillation (93-8° at 1.5 mm.) yielded V containing about 20% VII, satisfactory for producing VA. III (b18 75-80°) was prepared in 75% yield by refluxing I(CH2)2CO2H (36 g.) with 14 ml. PCl3 5 hrs. and distilling Using an ion exchange column (Cl form), I was converted to its dichloride, m. 200-1°. The dinitrate, m. 142°, and the dibitartrate, m. 123-6°, of I were prepared from I and the appropriate Ag salt. Picric acid and I yielded I dipicrate, m. 182-3°. In most examples, analyses are given.

IT 123935-68-2
(Derived from data in the 6th Collective Formula Index (1957-1961))

RN 123935-68-2 CAPLUS
CN Urea, 1-(2-diethylaminoethyl)-3-phenyl-1-(8-phenyl-3-nortropanyl)-2-thio-
(6CI) (CA INDEX NAME)



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